Electrical Conduction in Biological Tissues
Homogenization Techniques and Asymptotic Decay for Linear and Nonlinear Problems

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Abstract: We collect some results concerning electrical conduction problems in biological tissues. These problems are set in a finely mixed periodic medium and the unknown electric potentials solve standard elliptic equations set in different conductive regions (the intracellular and extracellular spaces), separated by an interface (the cell membrane), which exhibits both a capacitive and a conductive behavior. As the spatial period of the medium goes to zero, the problems approach a homogenization limit. The macroscopic models are obtained by using the technique of asymptotic expansions, in the case where the conductive behavior of the cell membrane is linear, and by means of two-scale convergence, in the case where, due to its biochemical structure, the cell membrane performs a strongly nonlinear conductive behavior. The asymptotic behavior of the macroscopic potential for large times is investigated, too.

1 INTRODUCTION

This is a review article concerning the results obtained by the authors in several papers dealing with some aspects of electrical conduction in biological tissues.

It is well known that electric potentials can be used in diagnostic devices to investigate the properties of biological tissues. Besides the well-known diagnostic techniques such as magnetic resonance, X-rays and so on, it plays an important role a more recent, cheap and noninvasive technique known as *electric impedance tomography* (EIT). Such a technique is essentially based on the possibility of determining the physiological properties of a living body by means of the knowledge of its electrical behavior.

This leads to an inverse problem for an elliptic equation, usually the Laplacian, which is the equation satisfied by the electrical potential, when the body is assumed to display only a resistive behavior. However, it has been observed that, applying high frequency potentials to the body, a capacitive behavior appears, due to the electric polarization at the interface of the cell membranes produced by the lipidic composition of the membranes themselves, which act as capacitors. This phenomenon (known in physics as Maxwell-Wagner effect) is studied modeling the biological tissue as a composite medium with a periodic microscopic structure of characteristic length ε, where two finely mixed conductive phases (the intra- and the extra-cellular phase) are separated by a dielectric interface (the cellular membrane). From the mathematical point of view, the electrical current flow through the tissue is described by means of a system of decoupled elliptic equations in the two conductive phases (obtained from the Maxwell equations, under the quasi-static assumption; i.e., we assume that the magnetic effects are negligible). The solutions of this system are coupled because of the interface conditions at the membrane, whose physical behavior is described by means of a dynamical boundary condition (which takes into account both the conductive and the capacitive behavior of the cell membrane), together with the flux-continuity assumption. Because of the complex geometry of the domain, these models are not easily handled, for example from the numerical point of view. This justifies the need of the homogenization approach, with the aim of producing macroscopic models for the whole medium as $\varepsilon \to 0$, since

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the typical scale ε of the microstructure is very small with respect to the tissue macroscopic scale analyzed in the experiments.

We present in the following two different cases: in the first one the conductive behavior of the cell membrane is assumed to be linear and the approach used in order to obtain the macroscopic equation is the asymptotic expansion introduced in (Bensoussan et al., 1978); in the second one, we assume a strongly nonlinear conductive behavior of the cell membrane, which actually appears in some physical situation and which is due to the presence of ionic channels, i.e. to the biochemical structure of the cell membrane itself. The technique used in this last case in order to obtain the effective potential of the tissue is the two-scale convergence technique introduced in (Nguetseng, 1989) and in (Allaire, 1992).

In the first case, the macroscopic equation obtained with this approach is an elliptic equation with memory, as it could be expected in any electrical circuit in which a capacitor is present. In the second case, we obtain a strictly coupled system of equations for the macroscopic and microscopic potentials, as usual when the two-scale convergence technique is applied.

2 SETTING OF THE PROBLEM

Let Ω be an open connected bounded subset of $\mathcal{R}^N$. Let us introduce a periodic open subset E of $\mathcal{R}^N$, so that $E + z = E$ for all $z \in Z^N$. For all $\varepsilon > 0$ define $\Omega^\varepsilon_{\text{int}} = \Omega \cap \varepsilon E$, $\Omega^\varepsilon_{\text{out}} = \Omega \setminus \overline{\varepsilon E}$. We assume that Ω, E have regular boundary, say of class C^∞ for the sake of simplicity. Moreover, we set $\Omega = \Omega^\varepsilon_{\text{int}} \cup \Omega^\varepsilon_{\text{out}} \cup \Gamma^\varepsilon$, where $\Gamma^\varepsilon = \partial\Omega^\varepsilon_{\text{int}} \cap \Omega = \partial\Omega^\varepsilon_{\text{out}} \cap \Omega$. We also employ the notation $Y = (0,1)^N$, and $E_{\text{int}} = E \cap Y$, $E_{\text{out}} = Y \setminus \overline{E}$, $\Gamma = \partial E \cap \overline{Y}$. As a simplifying assumption, we stipulate that E_{int} is a connected smooth subset of Y such that $\text{dist}(\overline{E_{\text{int}}}, \partial Y) > 0$. Some generalizations may be possible, but we do not dwell on this point here. Finally, we assume that $\text{dist}(\Gamma^\varepsilon, \partial\Omega) > \gamma\varepsilon$ for some constant $\gamma > 0$ independent of ε, by dropping the inclusions contained in the cells $\varepsilon(Y + z)$, $z \in Z^N$ which intersect $\partial\Omega$ (see Figure 1). Finally, let $T > 0$ be a given time.

We are interested in the homogenization limit as $\varepsilon \searrow 0$ of the problem for $u_\varepsilon(x,t)$ (here the operators div and ∇ act only with respect to the space variable x)

$$-\operatorname{div}(\sigma_{\text{int}} \nabla u_\varepsilon) = 0\,, \qquad \text{in } \Omega^\varepsilon_{\text{int}}; \qquad (1)$$

$$-\operatorname{div}(\sigma_{\text{out}} \nabla u_\varepsilon) = 0\,, \qquad \text{in } \Omega^\varepsilon_{\text{out}}; \qquad (2)$$

$$\sigma_{\text{int}} \nabla u^{(\text{int})}_\varepsilon \cdot \nu = \sigma_{\text{out}} \nabla u^{(\text{out})}_\varepsilon \cdot \nu\,, \qquad \text{on } \Gamma^\varepsilon; \qquad (3)$$

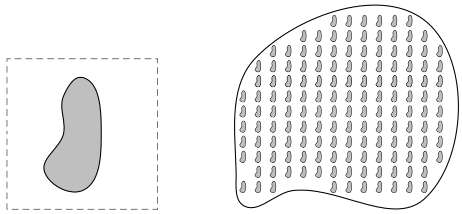

Figure 1: An examples of admissible periodic structures in $\mathcal{R}^2$. Left: Y is the dashed square, and $E \cap Y$ is the shaded region. Right: the domain Ω.

$$\frac{\alpha}{\varepsilon}\frac{\partial}{\partial t}[u_\varepsilon] + f\left(\frac{[u_\varepsilon]}{\varepsilon}\right) = \sigma_{\text{out}} \nabla u^{(\text{out})}_\varepsilon \cdot \nu\,, \qquad \text{on } \Gamma^\varepsilon; \quad (4)$$

$$[u_\varepsilon](x,0) = S_\varepsilon(x)\,, \qquad \text{on } \Gamma^\varepsilon; \quad (5)$$

$$u_\varepsilon(x,t) = 0\,, \qquad \text{on } \partial\Omega. \quad (6)$$

The notation in (1)–(4), (6), means that the indicated equations are in force in the relevant spatial domain for $0 < t < T$.

Here σ_{int}, σ_{out} and α are positive constants, and ν is the normal unit vector to Γ^ε pointing into $\Omega^\varepsilon_{\text{out}}$. Since u_ε is not in general continuous across Γ^ε we have set

$$u^{(\text{int})}_\varepsilon := \text{ trace of } u_{\varepsilon|\Omega^\varepsilon_{\text{int}}} \text{ on } \Gamma^\varepsilon;$$

$$u^{(\text{out})}_\varepsilon := \text{ trace of } u_{\varepsilon|\Omega^\varepsilon_{\text{out}}} \text{ on } \Gamma^\varepsilon.$$

Indeed we refer conventionally to $\Omega^\varepsilon_{\text{int}}$ as to the *interior domain*, and to $\Omega^\varepsilon_{\text{out}}$ as to the *outer domain*. We also denote

$$[u_\varepsilon] := u^{(\text{out})}_\varepsilon - u^{(\text{int})}_\varepsilon\,.$$

Similar conventions are employed for other quantities; for example (3) can be rewritten as

$$[\sigma \nabla u_\varepsilon \cdot \nu] = 0\,, \qquad \text{on } \Gamma^\varepsilon,$$

where

$$\sigma = \sigma_{\text{int}} \quad \text{in } \Omega^\varepsilon_{\text{int}}, \qquad \sigma = \sigma_{\text{out}} \quad \text{in } \Omega^\varepsilon_{\text{out}}.$$

The function f and the initial data S_ε will be discussed below.

Under the assumptions above, we prove existence and uniqueness of a weak solution to (1)–(6), in the class

$$u_{\varepsilon|\Omega^\varepsilon_i} \in L^2(0,T; H^1(\Omega^\varepsilon_i))\,, \qquad i = 1, 2\,, \qquad (7)$$

and $u_{\varepsilon|\partial\Omega} = 0$ in the sense of traces (Amar et al., 2005).

In the following, we will show that, if $\gamma^{-1}\varepsilon \leq S_\varepsilon(x) \leq \gamma\varepsilon$, where S_ε is the initial jump prescribed in (5), for a fixed constant $\gamma > 1$, then u_ε becomes stable as $\varepsilon \to 0$ (i.e., it converges to a nonvanishing bounded function). Therefore, let us stipulate that $S_\varepsilon \in H^{1/2}(\Gamma^\varepsilon)$ and

$$S_\varepsilon(x) = \varepsilon S_1\left(x, \frac{x}{\varepsilon}\right) + \varepsilon R_\varepsilon(x)\,, \qquad (8)$$

where $S_1 : \Omega \times \partial E \to \mathcal{R}$, and

$\|S_1\|_{L^\infty(\Omega\times\partial E)} < \infty , \qquad \|R_\varepsilon\|_{L^\infty(\Omega)} \to 0$, as $\varepsilon \to 0$;
$S_1(x,y)$ is continuous in x, uniformly over $y \in \partial E$, and periodic in y, for each $x \in \Omega$.

3 THE LINEAR CASE

In this section we assume that

$$f\left(\varepsilon^{-1}t\right) = \frac{\beta}{\varepsilon}t , \qquad t \in \mathcal{R} ,$$

with $\beta \geq 0$. Firstly, we remark that, up to a change of unknown function, we can assume $\beta = 0$; indeed, setting $v_\varepsilon(x,t) = u_\varepsilon(x,t) \cdot \exp\left(\frac{\beta}{\alpha}t\right)$, it follows that v_ε satisfies

$$\begin{aligned}
-\operatorname{div}(\sigma_{\mathrm{int}}\nabla v_\varepsilon) &= 0 , && \text{in } \Omega^\varepsilon_{\mathrm{int}};\\
-\operatorname{div}(\sigma_{\mathrm{out}}\nabla v_\varepsilon) &= 0 , && \text{in } \Omega^\varepsilon_{\mathrm{out}};\\
\sigma_{\mathrm{int}}\nabla v_\varepsilon^{(\mathrm{int})}\cdot\nu &= \sigma_{\mathrm{out}}\nabla v_\varepsilon^{(\mathrm{out})}\cdot\nu , && \text{on } \Gamma^\varepsilon;\\
\frac{\alpha}{\varepsilon}\frac{\partial}{\partial t}[v_\varepsilon] &= \sigma_{\mathrm{out}}\nabla v_\varepsilon^{(\mathrm{out})}\cdot\nu , && \text{on } \Gamma^\varepsilon;\\
[v_\varepsilon](x,0) &= S_\varepsilon(x) , && \text{on } \Gamma^\varepsilon;\\
v_\varepsilon(x,t) &= 0 , && \text{on } \partial\Omega.
\end{aligned}$$

Hence, from now on, we assume $\beta = 0$ in (4).

3.1 Homogenization

The weak formulation of Problem (1)–(6) is

$$\int_0^T\int_\Omega \sigma\nabla u_\varepsilon\cdot\nabla\psi\,\mathrm{d}x\,\mathrm{d}t - \frac{\alpha}{\varepsilon}\int_0^T\int_{\Gamma^\varepsilon}[u_\varepsilon]\frac{\partial}{\partial t}[\psi]\,\mathrm{d}\sigma\,\mathrm{d}t - \frac{\alpha}{\varepsilon}\int_{\Gamma^\varepsilon}[u_\varepsilon](0)[\psi](0)\,\mathrm{d}\sigma = 0 , \qquad (9)$$

for each $\psi \in L^2(\Omega\times(0,T))$ such that ψ is in the class (7), $[\psi] \in H^1(0,T;L^2(\Gamma^\varepsilon))$, and ψ vanishes on $\partial\Omega\times(0,T)$, as well as at $t = T$.

Moreover, multiplying (1), (2) by u_ε, integrating by parts and using (3)–(6), for all $0 < t < T$, we obtain the energy estimate

$$\int_0^t\int_\Omega \sigma|\nabla u_\varepsilon|^2\,\mathrm{d}x\,\mathrm{d}\tau + \frac{\alpha}{2\varepsilon}\int_{\Gamma^\varepsilon}[u_\varepsilon]^2(x,t)\,\mathrm{d}\sigma = \frac{\alpha}{2\varepsilon}\int_{\Gamma^\varepsilon}S_\varepsilon^2(x)\,\mathrm{d}\sigma \leq C < +\infty , \qquad (10)$$

where C does not depend on ε and the last inequality is due to (8), taking into account that $|\Gamma^\varepsilon|_{N-1} \sim 1/\varepsilon$.

Inequality (10) together with a suitable Poincaré type lemma assures that, up to a subsequence, $u_\varepsilon \to u$ weakly in $L^2\big(\Omega\times(0,T)\big)$. It remains to identify the limit function u, and this will be done in the following theorem.

Theorem 3.1. *Under the assumptions listed in Section 2, as $\varepsilon \to 0$, we have that $u_\varepsilon \to u$, weakly in $L^2(\Omega\times(0,T))$, and strongly in $L^1_{\mathrm{loc}}(0,T;L^1(\Omega))$, where the limit $u \in L^2(0,T;H^1_0(\Omega))$ solves in Ω*

$$-\operatorname{div}\left(\sigma_0\nabla_x u + A^0\nabla_x u + \int_0^t B(t-\tau)\nabla_x u(x,\tau)\,\mathrm{d}\tau\right) = \mathcal{F}$$

with $u = 0$ on $\partial\Omega$. Here $\mathcal{F}$ is a source depending on the initial condition S_1 in (8) and the two matrices A^0, B are symmetric and $A := \sigma_0 I + A^0$ is positive definite.

The proof of this theorem can be found in (Amar et al., 2003) and (Amar et al., 2004b) where $\mathcal{F}, A^0, B$ are explicitly defined.

Remark 3.2. In this regard, different models are obtained corresponding to different scaling with respect to ε (where ε denotes the length of the periodicity cell) of the relevant physical quantity α, entering in the dynamical interface condition given by

$$\frac{\alpha}{\varepsilon^k}\frac{\partial}{\partial t}[u_\varepsilon] = \sigma\nabla u_\varepsilon^{\mathrm{out}}\cdot\nu , \qquad \text{on } \Gamma^\varepsilon , \qquad (11)$$

with $k \in Z$. As we state in the previous theorem, the case $k = 1$ leads to an elliptic equation with memory, while the case $k = -1$ leads to a degenerate parabolic system, the well known bidomain model for the cardiac syncithial tissue (Krassowska and Neu, 1993), (Pennacchio et al., 2005). In turn, the case $k = 0$ leads to a standard elliptic equation (Lipton, 1998),(Amar et al., 2006).

In (Amar et al., 2006) we analyze in details the whole family $k \in Z$, proving that, for $k \geq 2$, the corresponding homogenized model reduces to a standard diffraction problem, while for $k \leq -2$, in the limit we obtain two independent standard Neumann problems.

We would like to observe that only the cases corresponding to $k = 1$ and $k = -1$ in (11), preserve memory, in the limit, of the membrane properties (i.e., of the constant α). This is not true for all the other choices of k.

It is not yet clear which one of these two models is more appropriate to describe the physical situation. Indeed, it seems that both of them are valid in their respective frequency ranges. However, the one presented here (i.e., model (1)–(6)) seems to be more suitable to describe the response of a biological tissue when high frequencies of alternating currents (of the order of Megahertz) are applied, since in this case the relevance of the capacitive properties of the dielectric membrane increases. In the case of frequencies of the order of hundreds of Megahertz an improved version of this model has been developed in (Amar et al., 2009b) and (Amar et al., 2010). On the contrary, the case $k=-1$ has been applied to low frequencies in the context of activation of cardiac muscle.

The applicability of this model to real physical situations is connected to the study of an inverse problem, which for the elliptic equation is tipically related to the study of the Neumann-Dirichlet map. This problem has been widely studied. On the contrary (apart from some geometrically simple cases), the inverse problem for the homogenized equation in Theorem 3.1 is still open; in this case, the usual Dirichlet-Neumann map should be replaced with a map in which we assign the Dirichlet boundary condition together with the condition:

$$\sigma_0\frac{\partial u}{\partial n}+A^0_{ij}\frac{\partial u}{\partial x_i}n_j+\int_0^t B_{ij}(t-\tau)\frac{\partial u}{\partial x_i}(x,\tau)n_j\,\mathrm{d}\tau=h(x,t)\,,$$

where n is the outward normal to $\partial\Omega$ and h is a given function.

3.2 Concentration of the Physical Problem

We point out that in the physical setting, the cell membrane has a nonzero thickness, even if it is very small with respect to the characteristic length of the cell. Hence, we denote by η the ratio between these two quantities and remark that $\eta << 1$. Moreover, we write Ω as $\Omega=\Omega^{\varepsilon,\eta}\cup\Gamma^{\varepsilon,\eta}\cup\partial\Gamma^{\varepsilon,\eta}$, where $\Omega^{\varepsilon,\eta}$ and $\Gamma^{\varepsilon,\eta}$ are two disjoint open subsets of Ω, $\Gamma^{\varepsilon,\eta}$ is the tubular neighborhood of Γ^{ε} with thickness $\varepsilon\eta$, and $\partial\Gamma^{\varepsilon,\eta}$ is its boundary. In addition, we assume also that $\Omega^{\varepsilon,\eta}=\Omega^{\varepsilon,\eta}_{\mathrm{int}}\cup\Omega^{\varepsilon,\eta}_{\mathrm{out}}$ and $\partial\Gamma^{\varepsilon,\eta}=(\partial\Omega^{\varepsilon,\eta}_{\mathrm{int}}\cup\partial\Omega^{\varepsilon,\eta}_{\mathrm{out}})\cap\Omega$. Again, $\Omega^{\varepsilon,\eta}_{\mathrm{out}}$, $\Omega^{\varepsilon,\eta}_{\mathrm{int}}$ correspond to the conductive regions, and $\Gamma^{\varepsilon,\eta}$ to the dielectric shell. We assume that, for $\eta\to 0$ and $\varepsilon>0$ fixed, $|\Gamma^{\varepsilon,\eta}|\sim\varepsilon\eta|\Gamma^{\varepsilon}|_{N-1}$, $\Omega^{\varepsilon,\eta}\to\Omega^{\varepsilon}_{\mathrm{out}}\cup\Omega^{\varepsilon}_{\mathrm{int}}$ and $\partial\Gamma^{\varepsilon,\eta}\to\Gamma^{\varepsilon}$. We employ also the notation $Y=E^{\eta}\cup\Gamma^{\eta}\cup\partial\Gamma^{\eta}$, where E^{η} and Γ^{η} are two disjoint open subsets of Y, Γ^{η} is the tubular neighborhood of Γ with thickness η, and $\partial\Gamma^{\eta}$ is its boundary. Moreover, $E^{\eta}=E^{\eta}_{\mathrm{int}}\cup E^{\eta}_{\mathrm{out}}$ (see Figure 2). For $\eta\to 0$, $E^{\eta}\to E_{\mathrm{int}}\cup E_{\mathrm{out}}$, $|\Gamma^{\eta}|\sim\eta|\Gamma|_{N-1}$ and $\partial\Gamma^{\eta}\to\Gamma$.

The classical governing equation is derived from the Maxwell system in the quasi-static approximation, which gives

$$-\operatorname{div}(A^{\eta}\nabla u^{\eta}_{\varepsilon})=0\,,\qquad \text{in } \Omega^{\varepsilon,\eta}; \tag{12}$$

$$-\operatorname{div}(B^{\eta}\nabla u^{\eta}_{\varepsilon t})=0\,,\qquad \text{in } \Gamma^{\varepsilon,\eta}; \tag{13}$$

$$A^{\eta}\nabla u^{\eta}_{\varepsilon}\cdot\nu^{\eta}=B^{\eta}\nabla u^{\eta}_{\varepsilon t}\cdot\nu^{\eta}\,,\qquad \text{on } \partial\Gamma^{\varepsilon,\eta}; \tag{14}$$

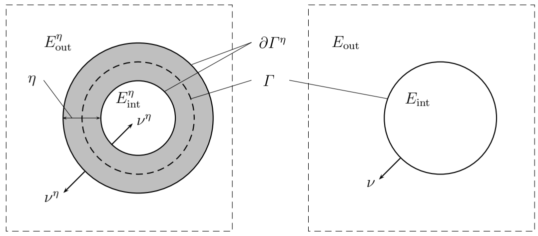

Figure 2: The periodic cell Y. *Left*: before concentration; Γ^{η} is the shaded region, and $E^{\eta}=E^{\eta}_{\mathrm{int}}\cup E^{\eta}_{\mathrm{out}}$ is the white region. *Right*: after concentration; Γ^{η} shrinks to Γ as $\eta\to 0$.

$$\nabla u^{\eta}_{\varepsilon}(x,0)=\mathcal{S}^{\eta}_{\varepsilon}(x)\,,\qquad \text{in } \Gamma^{\varepsilon,\eta}; \tag{15}$$

$$u^{\eta}_{\varepsilon}(x,t)=0\,,\qquad \text{on } \partial\Omega. \tag{16}$$

We assume that the conductivity $A^{\eta}>0$ is such that $A^{\eta}=\sigma_{\mathrm{int}}$ in $\Omega^{\varepsilon,\eta}_{\mathrm{int}}$, $A^{\eta}=\sigma_{\mathrm{out}}$ in $\Omega^{\varepsilon,\eta}_{\mathrm{out}}$; the permeability $B^{\eta}>0$ is such that $B^{\eta}=\alpha\eta$; and $\mathcal{S}^{\eta}_{\varepsilon}=\nabla\widetilde{S}^{\eta}_{\varepsilon}$, for some $\widetilde{S}^{\eta}_{\varepsilon}\in H^1(\Gamma^{\varepsilon,\eta})$ with $|\mathcal{S}^{\eta}_{\varepsilon}|\sim 1/\eta$.

Remark 3.3. We are interested in preserving, in the limit $\eta\to 0$, the conduction *across* the membrane Γ^{ε} instead of the *tangential* conduction on Γ^{ε}. To this purpose, we need to preserve the flux $B^{\eta}\nabla u^{\eta}_{\varepsilon t}\cdot\nu$ and the jump $[u^{\eta}_{\varepsilon t}]$ across the dielectric shells to be concentrated. This is the reason for which we rescale $B^{\eta}=\alpha\eta$, instead of scaling $B^{\eta}=\alpha/\eta$ in $\Gamma^{\varepsilon,\eta}$, as more usual in concentrated-capacity literature.

We are next interested in passing to the limit for $\eta\to 0^+$, keeping $\varepsilon>0$ fixed. In (Amar et al., 2006) we proved the following result.

Theorem 3.4. *Under the previous assumptions, when* $\eta\to 0^+$, *it follows that the concentration of Problem* (12)–(16) *is given by* (1)–(6) *(with* $f\equiv 0$*). More precisely, as* $\eta\to 0^+$ *it follows that* $u^{\eta}_{\varepsilon}\to u_{\varepsilon}$*, weakly in* $L^2_{\mathrm{loc}}(\Omega\times(0,T))$*, where* $u_{\varepsilon|\Omega^{\varepsilon}_{\mathrm{int}}}\in L^2_{\mathrm{loc}}(0,T;H^1(\Omega^{\varepsilon}_{\mathrm{int}}))$, $u_{\varepsilon|\Omega^{\varepsilon}_{\mathrm{out}}}\in L^2_{\mathrm{loc}}(0,T;H^1(\Omega^{\varepsilon}_{\mathrm{out}}))$ *and* u_{ε} *is the unique solution of* (1)–(6) *(with* $f\equiv 0$*). Moreover, as* $\eta\to 0^+$, $\nabla u^{\eta}_{\varepsilon}\to\nabla u_{\varepsilon}$*, weakly in* $L^2_{\mathrm{loc}}(\Omega^{\varepsilon}_{\mathrm{int}}\times(0,T))$ *and in* $L^2_{\mathrm{loc}}(\Omega^{\varepsilon}_{\mathrm{out}}\times(0,T))$.

3.3 Well-posedness Results

The first result of this section is connected with the existence and uniqueness of the solution of the microscopic problem; hence ε is assumed to be fixed and equal to 1.

Theorem 3.5. *Let* Ω *be an open connected bounded subset of* $\mathcal{R}^N$ *such that* $\Omega=\Omega_1\cup\Omega_2\cup\Gamma$*, where* Ω_1 *and* Ω_2 *are two disjoint open subset of* Ω, $\Gamma=\overline{\partial\Omega_1\cap\Omega}=\overline{\partial\Omega_2\cap\Omega}$ *is a compact regular set, and* $\Gamma\cap\partial\Omega=\emptyset$*. Assume also that* Ω, Ω_1 *and* Ω_2 *have Lipschitz boundaries. Let* $\alpha>0$ *and* $\beta\geq 0$*. Let*

$f \in L^2(\Omega \times (0,T))$, $q,h \in L^2(0,T;L^2(\Gamma))$, and $S \in H^{1/2}(\Gamma)$. Therefore, problem

$$-\sigma \Delta v = f(t)\,, \qquad \text{in } \Omega_1, \Omega_2; \tag{17}$$

$$[\sigma \nabla v \cdot \nu] = q(t)\,, \qquad \text{on } \Gamma; \tag{18}$$

$$\alpha \frac{\partial}{\partial t}[v] = \sigma_{\text{out}} \nabla v^{(\text{out})} \cdot \nu + h(t)\,, \qquad \text{on } \Gamma; \tag{19}$$

$$[v](x,0) = S\,, \qquad \text{on } \Gamma; \tag{20}$$

$$v(x,t) = 0\,, \qquad \text{on } \partial\Omega; \tag{21}$$

admits a unique solution $v \in L^2(0,T;\mathcal{H}^1_o(\Omega))$ with $[v] \in C(0,T;L^2(\Gamma))$, where $\mathcal{H}^1_o(\Omega) = \{u = (u_1,u_2) \mid u_1 := u_{|\Omega_{\text{int}}}, u_2 := u_{|\Omega_{\text{out}}}$ with $u_1,u_2 \in H^1_o(\Omega)\}$.

The technique employed to prove this theorem relies on a result of existence and uniqueness for abstract parabolic equations, to which Problem (17)–(21) can be reduced by means of a suitable identification of the function spaces there involved (Zeidler, 1990, Chapter 23). For the details see (Amar et al., 2005).

Remark 3.6. Note that the same result as in Theorem 3.5 holds if we assume that $\Omega = Y = (0,1)^N$, $g(\cdot,t)$ is Y-periodic for a.e. $t \in (0,T)$, f and q satisfy the compatibility condition

$$\int_Y f(y,t)\,dy = \int_\Gamma q(y,t)\,dy \qquad \text{for a.e. } t \in (0,T)\,,$$

and we replace (21) with the requirement that $v(\cdot,t)$ is Y-periodic.

For the homogenized problem an existence and uniqueness theorem, both for weak and classical solutions, is available.

Theorem 3.7. *Let $A \in L^\infty(\Omega;\mathcal{R}^{N^2})$ be a symmetric matrix such that $\lambda|\xi|^2 \le A(x)\xi\cdot\xi \le \Lambda|\xi|^2$, for suitable $0 < \lambda < \Lambda < +\infty$, for almost every $x \in \Omega$ and every $\xi \in \mathcal{R}^N$; let $B \in L^2(0,T;L^\infty(\Omega;\mathcal{R}^{N^2}))$, and let $g \in L^2(0,T;H^1(\Omega))$. Assume that $f : \Omega \times (0,T) \to \mathcal{R}$ is a Carathéodory function such that $f \in L^2(0,T;H^{-1}(\Omega))$ and $g \in L^2(0,T;H^1(\Omega))$.*

Then, there exists a unique function $u \in L^2(0,T;H^1(\Omega))$ satisfying in the sense of distributions

$$-\operatorname{div}\left(A(x)\nabla_x u + \int_0^t B(x,t-\tau)\nabla_x u(x,\tau)\,d\tau\right) = f(x,t)$$

in $\Omega \times (0,T)$ with $u = g$ on $\partial\Omega \times (0,T)$.

Theorem 3.8. *Let $m \ge 0$ be any fixed integer and let also $0 < \gamma < 1$. Let $A \in C^{1+\gamma}(\overline{\Omega};\mathcal{R}^{N^2})$ satisfy the assumption of Theorem 3.7 and*

$$B \in C^0([0,T];C^{1+\gamma}(\overline{\Omega};\mathcal{R}^{N^2}))$$

be such that

$$B' \in L^2(0,T;W^{1,\infty}(\Omega;\mathcal{R}^{N^2}))\,.$$

Assume that $f \in C^0([0,T];C^{m+\gamma}(\overline{\Omega}))$, and that $\nabla_x f(x,t)$ and $f_t(x,t)$ exist and are bounded. Let $g \in C^0([0,T];C^{m+2+\gamma}(\overline{\Omega}))$, with $g_t \in L^\infty(0,T;C^{m+2+\gamma}(\overline{\Omega}))$.

Then the solution u given in Theorem 3.8 belongs to $C^0([0,T];C^{1+\gamma}(\overline{\Omega})) \cap L^\infty(0,T;C^{m+2+\gamma}(\overline{\Omega}))$ and solves the problem in the classical sense.

Both the proofs can be obtained, for example, with a standard delay argument or a fixed point theorem, together with an a-priori estimate in the corresponding function spaces. The a-priori estimates are obtained as in standard elliptic equations, using also the Gronwall's Theorem to deal with the memory term (Amar et al., 2004a).

3.4 Stability

In this section we will give a brief description of the asymptotic behavior of $u_\varepsilon(x,t)$ and $u(x,t)$ for large times. The interest in studying the asymptotics of this model is due to the fact that the diagnostic measurements are in general performed at times significantly longer than the typical relaxation time of the system.

In the case where a homogeneous Dirichlet boundary condition is satisfied, the following results were proven in (Amar et al., 2009a).

Theorem 3.9. *Let $\Omega^\varepsilon_{\text{int}}, \Omega^\varepsilon_{\text{out}}, \Gamma^\varepsilon, \sigma_{\text{int}}, \sigma_{\text{out}}, \alpha$ be as before. Assume that the initial datum S_ε satisfies* (8). *Let u_ε be the solution of* (1)–(6) *(with $f \equiv 0$). Then*

$$\|u_\varepsilon(\cdot,t)\|_{L^2(\Omega)} \le C(\varepsilon + e^{-\lambda t}) \quad \text{a.e. in } (1,+\infty), \tag{22}$$

where C and λ are independent of ε. Moreover, if S_ε has null mean average over each connected component of Γ^ε, it follows that

$$\|u_\varepsilon(\cdot,t)\|_{L^2(\Omega)} \le Ce^{-\lambda t} \quad \text{a.e. in } (1,+\infty). \tag{23}$$

This theorem easily yields the following exponential time-decay estimate for u under homogeneous Dirichlet boundary data.

Corollary 3.10. *Under the assumptions of Theorem 3.9, if $u_\varepsilon \to u$ weakly in $L^2(\Omega \times (0,\overline{T}))$ for every $\overline{T} > 0$, then*

$$\|u(\cdot,t)\|_{L^2(\Omega)} \le Ce^{-\lambda t} \quad \text{a.e. in } (1,+\infty). \tag{24}$$

Next we are interested in the case of a nonhomogeneous but time-periodic Dirichlet boundary data for u_ε and u. Then we assume

$$u_\varepsilon(x,t) = \Psi(x)\Phi(t) \qquad \text{and} \qquad u(x,t) = \Psi(x)\Phi(t)\,, \tag{25}$$

on $\partial\Omega \times (0,+\infty)$, where

$$\Phi(t) \in H^1_\#(\mathcal{R})\,, \qquad \Psi(x) \in H^1(\mathcal{R}^N)\,, \qquad \Delta\Psi = 0 \tag{26}$$

in Ω. Here and in the following a subscript # denotes a space of T-periodic functions, for some fixed $T > 0$.

In order to deal with this case, for every $\varepsilon > 0$ we introduce an auxiliary function $u_\varepsilon^\#$ which solves a time-periodic version of the microscopic differential scheme introduced in Section 2

$$-\operatorname{div}(\sigma\nabla u_\varepsilon^\#) = 0\,, \qquad \text{in } (\Omega_{\text{int}}^\varepsilon \cup \Omega_{\text{out}}^\varepsilon) \times \mathcal{R}; \quad (27)$$

$$[\sigma\nabla u_\varepsilon^\# \cdot \nu] = 0\,, \qquad \text{on } \Gamma^\varepsilon \times \mathcal{R}; \quad (28)$$

$$\frac{\alpha}{\varepsilon}\frac{\partial}{\partial t}[u_\varepsilon^\#] = \sigma\nabla u_\varepsilon^{\#,\text{out}} \cdot \nu\,, \qquad \text{on } \Gamma^\varepsilon \times \mathcal{R}; \quad (29)$$

$$u_\varepsilon^\#(x,t) = \Psi(x)\Phi(t)\,, \qquad \text{on } \partial\Omega \times \mathcal{R}; \quad (30)$$

$$u_\varepsilon^\#(x,\cdot) \text{ is } T \text{ periodic}, \qquad \forall x \in \Omega; \quad (31)$$

$$[u_\varepsilon^\#(\cdot,t)] - S_\varepsilon(\cdot) \text{ has null average over each connected component of } \Gamma^\varepsilon. \quad (32)$$

Indeed, this problem is derived from (1)–(6) (with $f \equiv 0$), replacing equation (5) with (31). Equation (32) has been added in order to guarantee the uniqueness of the solution, and is suggested by the observation that $[u_\varepsilon(\cdot,t)] - S_\varepsilon(\cdot)$ has null average over each connected component of Γ^ε, as a consequence of (1)–(4), (5).

In (Amar et al., 2009a, Theorem 7) it has been proved that as $\varepsilon \to 0$, the function $u_\varepsilon^\#(x,t)$ approaches a time-periodic function $u^\# \in H_\#^1(\mathcal{R}; H^1(\Omega))$ solving

$$-\operatorname{div}\left(A\nabla u^\# + \int_0^{+\infty} B(\tau)\nabla u^\#(x,t-\tau)\,\mathrm{d}\tau\right) = 0\,, \quad (33)$$

in $\Omega \times \mathcal{R}$, with $u^\# = \Psi(x)\Phi(t)$ on $\partial\Omega \times \mathcal{R}$. Here A and B the same matrices defined in Theorem 3.1.

Moreover, the following result holds.

Theorem 3.11. *Let $\Omega_{\text{int}}^\varepsilon, \Omega_{\text{out}}^\varepsilon, \Gamma^\varepsilon$, $\sigma_{\text{int}}, \sigma_{\text{out}}, \alpha$ be as before. Assume that the initial datum S_ε satisfies* (8) *and the boundary datum satisfies* (26)*. Let $\{u_\varepsilon\}$ and $\{u_\varepsilon^\#\}$ be the sequences of the solutions of* (1)–(5) *(with $f \equiv 0$),* (25) *and* (27)–(32)*, respectively. Then*

$$\|u_\varepsilon(\cdot,t) - u_\varepsilon^\#(\cdot,t)\|_{L^2(\Omega)} \le Ce^{-\lambda t} \quad \textit{a.e. in } (1,+\infty),$$

where C and λ are positive constants, independent of ε.

This theorem easily yields the following exponential time-decay estimate for $u - u^\#$.

Corollary 3.12. *Under the assumption of Theorem 3.11, if $u_\varepsilon \to u$ and $u_\varepsilon^\# \to u^\#$ weakly in $L^2(\Omega \times (0,\overline{T}))$, for every $\overline{T} > 0$, then the following estimate holds:*

$$\|u(\cdot,t) - u^\#(\cdot,t)\|_{L^2(\Omega)} \le Ce^{-\lambda t} \quad \textit{a.e. in } (1,+\infty),$$

where C and λ are positive constants, independent of ε.

Finally, expressing the function Φ by means of its Fourier series; i.e.,

$$\Phi(t) = \sum_{k=-\infty}^{+\infty} c_k \mathrm{e}^{i\omega_k t} \quad (34)$$

where $\omega_k = 2k\pi/T$ is the k-th circular frequency, and representing the solution $u_\varepsilon^\#(x,t)$ as follows:

$$u_\varepsilon^\#(x,t) = \sum_{k=-\infty}^{+\infty} v_{\varepsilon k}(x)\mathrm{e}^{i\omega_k t}\,, \quad (35)$$

we obtain that the complex-valued functions $v_{\varepsilon k}(x) \in L^2(\Omega)$ are such that $v_{\varepsilon k}|_{\Omega_i^\varepsilon} \in H^1(\Omega_i^\varepsilon)$, $i = 1,2$, and for $k \neq 0$ satisfy the problem

$$-\operatorname{div}(\sigma\nabla v_{\varepsilon k}) = 0\,, \qquad \text{in } \Omega_{\text{int}}^\varepsilon \cup \Omega_{\text{out}}^\varepsilon; \quad (36)$$

$$[\sigma\nabla v_{\varepsilon k} \cdot \nu] = 0\,, \qquad \text{on } \Gamma^\varepsilon; \quad (37)$$

$$\frac{i\omega_k\alpha}{\varepsilon}[v_{\varepsilon k}] = (\sigma\nabla v_{\varepsilon k} \cdot \nu)^{\text{out}}\,, \qquad \text{on } \Gamma^\varepsilon; \quad (38)$$

$$v_{\varepsilon k} = c_k\Psi\,, \qquad \text{on } \partial\Omega, \quad (39)$$

whereas for $k = 0$ they satisfy the problem

$$-\operatorname{div}(\sigma\nabla v_{\varepsilon 0}) = 0\,, \quad \text{in } \Omega_{\text{int}}^\varepsilon \cup \Omega_{\text{out}}^\varepsilon; \quad (40)$$

$$[\sigma\nabla v_{\varepsilon 0} \cdot \nu] = 0\,, \qquad \text{on } \Gamma^\varepsilon; \quad (41)$$

$$(\sigma\nabla v_{\varepsilon 0} \cdot \nu)^{\text{out}} = 0\,, \qquad \text{on } \Gamma^\varepsilon; \quad (42)$$

$$v_{\varepsilon 0} = c_0\Psi\,, \qquad \text{on } \partial\Omega; \quad (43)$$

$$[v_{\varepsilon 0}] - S_\varepsilon(\cdot) \text{ has null average over each connected component of } \Gamma^\varepsilon. \quad (44)$$

Note that any solution $v_{\varepsilon k}$ of Problem (36)–(39) is such that $[v_{\varepsilon k}]$ has null average over each connected component of Γ^ε.

Finally, in (Amar et al., 2009a) the following homogenization result is proven:

Theorem 3.13. *Let $\Omega_{\text{int}}^\varepsilon, \Omega_{\text{out}}^\varepsilon, \Gamma^\varepsilon$, $\sigma_{\text{int}}, \sigma_{\text{out}}, \alpha$ be as before. Assume that the boundary datum satisfies* (26)*. Then, for $k \in Z \setminus \{0\}$ [respectively, $k = 0$, under the further assumptions* (8)*, the solution $v_{\varepsilon k}$ of Problem* (36)–(39) *[respectively, Problem* (40)–(44)*] strongly converges in $L^2(\Omega)$ to a function $v_{0k} \in H^1(\Omega)$ which is the unique solution of the problem*

$$-\operatorname{div}(A^{\omega_k}\nabla v_{0k}) = 0\,, \qquad \textit{in } \Omega; \quad (45)$$

$$v_{0k} = c_k\Psi\,, \qquad \textit{on } \partial\Omega; \quad (46)$$

where

$$A^{\omega_k} = A + \int_0^{+\infty} B(t)\,e^{-i\omega_k t}\,\mathrm{d}t\,, \quad (47)$$

with A and B the same matrices defined in Theorem 3.1.

Remark 3.14. Experimental measurements in clinical applications are currently performed by assigning time-harmonic boundary data and assuming that the resulting electric potential is time-harmonic, too. This assumption, which is often referred to as the limiting amplitude principle, leads to the commonly accepted mathematical model based on the complex elliptic Problem (45)–(46) for the electric potential (Borcea, 2003), (Dehghani and Soni, 2005). In (Amar et al., 2009a), in view of the preceding theorem, this phenomenological equations have been mathematically justified and, moreover, in (47) a quasi-explicit relation between the circular frequency ω_k and the coefficient A^{ω_k} has been found.

4 THE NONLINEAR CASE

In this section the function f appearing in equation (4) is assumed to be continuous and strictly monotone increasing; moreover, we require that $f(0)=0$ and $|f(s)|\leq\Lambda|s|\quad\forall s\in\mathcal{R}$, where $\Lambda>0$ is a suitable constant. For later use, let us set

$$\mathcal{X}^1_\#(Y):=\{(u^{(1)},u^{(2)})\mid u^{(1)}:=u_{|E_{\mathrm{int}}},u^{(2)}:=u_{|E_{\mathrm{out}}},$$
$$\text{with } u^{(1)}\in H^1(E_1)\,,\ u^{(2)}\in H^1(E_2)\,,\ \text{and } u\,Y-\text{periodic}\}\,,$$

and recall the definition of two-scale convergence.

Definition 4.1. Given a sequence $\{u_\varepsilon\}\in L^2\big(0,T;L^2(\Omega)\big)$ and a function $u\in L^2\big(0,T;L^2(\Omega\times Y)\big)$, we say that u_ε two-scale converges to u in $L^2\big(0,T;L^2(\Omega\times Y)\big)$ for $\varepsilon\to0$ (and we write $u_\varepsilon\overset{2-sc}{\to}u$) if

$$\lim_{\varepsilon\to0}\int_0^T\int_\Omega u_\varepsilon(x,t)\varphi\left(x,\frac{x}{\varepsilon},t\right)\mathrm{d}x\,\mathrm{d}t=$$
$$\int_0^T\int_{\Omega\times Y}u(x,y,t)\varphi(x,y,t)\,\mathrm{d}x\,\mathrm{d}y\,\mathrm{d}t$$

for any test function $\varphi\in L^2_\#\big(Y;\mathcal{C}(\overline{\Omega}\times[0,T])\big)$.

Following (Allaire et al., 1995) (see also (Hummel, 2000)), we recall also the notion of two-scale convergence for sequences of functions defined on periodic surfaces, suitably adapted to the time-dependent case.

Definition 4.2. Given a sequence $\{v_\varepsilon\}\in L^2\big(0,T;L^2(\Gamma^\varepsilon)\big)$ and a function $v\in L^2\big(\Omega\times(0,T);L^2(\Gamma)\big)$, we say that v_ε two-scale converges to v in $L^2\big(\Omega\times(0,T);L^2(\Gamma)\big)$ for $\varepsilon\to0$ (and we write $v_\varepsilon\overset{2-sc}{\to}v$) if

$$\lim_{\varepsilon\to0}\varepsilon\int_0^T\int_{\Gamma^\varepsilon}v_\varepsilon(x,t)\psi\left(x,\frac{x}{\varepsilon},t\right)\mathrm{d}\sigma\,\mathrm{d}t=$$
$$\int_0^T\int_\Omega\int_\Gamma v(x,y,t)\psi(x,y,t)\,\mathrm{d}x\,\mathrm{d}\sigma(y)\,\mathrm{d}t$$

for any test function $\psi\in\mathcal{C}\big(\overline{\Omega}\times[0,T];\mathcal{C}_\#(Y)\big)$.

A weak formulation and an energy estimate analogous to the ones in (9) and (10) can be written down also in this case, so that we can assert again that, up to a subsequence, $u_\varepsilon\to u$ weakly in $L^2\big(\Omega\times(0,T)\big)$, where u is identified in the next theorem (see (Amar et al., 2013a)).

Theorem 4.3. *Let the assumptions listed in Section 2 be satisfied and let f be as stated above. Assume, in addition, that $S_\varepsilon/\varepsilon$ two-scale converges in $L^2\big(\Omega;L^2(\Gamma)\big)$ to a function S_1 which satisfies $S_1(x,\cdot)=S_{|\Gamma}(x,\cdot)$ for some $S\in\mathcal{C}\big(\overline{\Omega};\mathcal{C}^1_\#(Y)\big)$, and*

$$\lim_{\varepsilon\to0}\varepsilon\int_{\Gamma^\varepsilon}\left(\frac{S_\varepsilon}{\varepsilon}\right)^2(x)\,\mathrm{d}\sigma=\int_\Omega\int_\Gamma S_1^2(x,y)\,\mathrm{d}x\,\mathrm{d}\sigma(y)\,.$$

Then there exists $u\in L^2\big(0,T;H^1_o(\Omega)\big)$ and there exists $u_1\in L^2\big(\Omega\times(0,T);\mathcal{X}^1_\#(Y)\big)$ such that, as $\varepsilon\to0$, we have

$$u_\varepsilon\to u\qquad\text{strongly in } L^2_{loc}\big(0,T;L^2(\Omega)\big),$$
$$1_{\Omega\setminus\Gamma^\varepsilon}\nabla u_\varepsilon\overset{2-sc}{\to}\nabla u+\nabla_y u_1\qquad\text{in } L^2\big(0,T;L^2(\Omega\times Y)\big),$$
$$\varepsilon^{-1}[u_\varepsilon]\overset{2-sc}{\to}[u_1]\qquad\text{in } L^2\big(\Omega\times(0,T);L^2(\Gamma)\big).$$

Moreover, the pair (u,u_1) solves

$$-\operatorname{div}\left(\sigma_0\nabla u+\int_Y\sigma\nabla_y u_1\,\mathrm{d}y\right)=0\,,\qquad\text{in }\Omega;\quad(48)$$

$$-\operatorname{div}_y(\sigma\nabla u+\sigma\nabla_y u_1)=0\,,\ \text{in }\Omega\times(E_{\mathrm{int}}\cup E_{\mathrm{out}});\quad(49)$$

$$[\sigma(\nabla u+\nabla_y u_1)\cdot\nu]=0\,,\qquad\text{on }\Omega\times\Gamma;\quad(50)$$

$$\alpha\frac{\partial}{\partial t}[u_1]+f([u_1])=\sigma(\nabla u+\nabla_y u_1)\cdot\nu\,,\quad\text{on }\Omega\times\Gamma;\quad(51)$$

$$[u_1](x,y,0)=S_1(x,y)\,,\qquad\text{on }\Omega\times\Gamma;\quad(52)$$

$$u(x,t)=0\,,\qquad\text{on }\partial\Omega.\quad(53)$$

As in Subsection 3.4, also in this nonlinear case we are interested in studying the asymptotic behavior of the macroscopic potential u for large times. In the case where a homogeneous Dirichlet boundary condition is satisfied, the following result is proven in (Amar et al., 2013b, in preparation), which is analogous to the one stated in Corollary 3.10.

Theorem 4.4. *Let u,u_1 be the solution of the homogenized Problem* (48)–(53)*. Then,*

$$\|u(\cdot,t)\|_{L^2(\Omega)}\leq Ce^{-\lambda t}\quad\text{a.e. in }(1,+\infty)$$

5 CONCLUSIONS AND FUTURE PERSPECTIVES

As already pointed out in Remark 3.14 our research gives, at least in the linear case, a mathematical justification of the phenomenological model (45)–(46) commonly accepted in clinical applications, when time-harmonic boundary data are assigned (Borcea, 2003), (Dehghani and Soni, 2005). At the same time, in (47) a quasi-explicit relation between the circular frequency ω_k and the coefficient A^{ω_k} has been found. Moreover, we provide also a model for the case of general periodic boundary data (see (33)). These results could be useful in clinical applications for the reduction of the noise problems still affecting the diagnostic image reconstruction.

Our future research will be mainly aimed at obtaining similar results also in the nonlinear case where, at present, the asymptotic behavior of the electric potential, when time-harmonic or periodic boundary data are assigned, has not completely been exploited.

REFERENCES

Allaire, G. (1992). Homogenization and two-scale convergence. *SIAM J. Math. Anal.*, 23:1482–1518.

Allaire, G., Damlamian, A., and Hornung, U. (1995). Two-scale convergence on periodic surfaces and applications. *Proceedings of the International Conference on Mathematical Modelling of Flow through Porous Media*, pages 15–25.

Amar, M., Andreucci, D., Bisegna, P., and Gianni, R. (2003). Homogenization limit for electrical conduction in biological tissues in the radio-frequency range. *Comptes Rendus Mecanique*, 331:503–508.

Amar, M., Andreucci, D., Bisegna, P., and Gianni, R. (2004a). An elliptic equation with history. *C. R. Acad. Sci. Paris, Ser. I*, 338:595–598.

Amar, M., Andreucci, D., Bisegna, P., and Gianni, R. (2004b). Evolution and memory effects in the homogenization limit for electrical conduction in biological tissues. *Mathematical Models and Methods in Applied Sciences*, 14:1261–1295.

Amar, M., Andreucci, D., Bisegna, P., and Gianni, R. (2005). Existence and uniqueness for an elliptic problem with evolution arising in electrodynamics. *Nonlinear Analysis Real World Applications*, 6:367–380.

Amar, M., Andreucci, D., Bisegna, P., and Gianni, R. (2006). On a hierarchy of models for electrical conduction in biological tissues. *Mathematical Methods in the Applied Sciences*, 29:767–787.

Amar, M., Andreucci, D., Bisegna, P., and Gianni, R. (2009a). Exponential asymptotic stability for an elliptic equation with memory arising in electrical conduction in biological tissues. *Euro. Jnl. of Applied Mathematics*, 20:431–459.

Amar, M., Andreucci, D., Bisegna, P., and Gianni, R. (2009b). Stability and memory effects in a homogenized model governing the electrical conduction in biological tissues. *J. Mechanics of Material and Structures*, (2) 4:211–223.

Amar, M., Andreucci, D., Bisegna, P., and Gianni, R. (2010). Homogenization limit and asymptotic decay for electrical conduction in biological tissues in the high radiofrequency range. *Communications on Pure and Applied Analysis*, (5) 9:1131–1160.

Amar, M., Andreucci, D., Bisegna, P., and Gianni, R. (2013a). A hierarchy of models for the electrical conduction in biological tissues via two-scale convergence: the nonlinear case. *Diff. and Int. Equations*. to appear.

Amar, M., Andreucci, D., Bisegna, P., and Gianni, R. (2013b). in preparation. in preparation.

Bensoussan, A., Lions, J., and G.Papanicolaou (1978). *Asymptotic Analysis for Periodic Structures*. North Holland, Amsterdam.

Borcea, L. (2003). Electrical impedance tomography. *Inverse Problems*, 18:R99–R136.

Dehghani, H. and Soni, N. (2005). Electrical impedance spectroscopy: theory. pages 85–105.

Hummel, H.-K. (2000). Homogenization for heat transfer in polycrystals with interfacial resistances. *Appl. Anal.*, 75:403–424.

Krassowska, W. and Neu, J. C. (1993). Homogenization of syncytial tissues. *Critical Reviews in Biomedical Engineering*, 21:137–199.

Lipton, R. (1998). Heat conduction in fine scale mixtures with interfacial contact resistance. *SIAM Journal of Applied Mathematics*, 58:55–72.

Nguetseng, G. (1989). A general convergence result for a functional related to the theory of homogenization. *SIAM J. Math. Anal.*, 20:608–623.

Pennacchio, M., Colli Franzone, P., and Savarè, G. (2005). Multiscale modeling for the electric activity of the heart. *Siam J. Math. Anal.*, 37:1333–1370.

Zeidler, E. (1990). *Nonlinear Functional Analysis and its Applications*, volume II A and II B. Springer Verlag, New York.