Homogenization limit for electrical conduction in biological tissues in the radio-frequency range

Micol Amar [a,1] Daniele Andreucci [a,2] Paolo Bisegna [b,2]
Roberto Gianni [a,2]

[a] *Dipartimento di Metodi e Modelli Matematici*
Università di Roma "La Sapienza"
via A.Scarpa 16, 00161 Roma, Italy

[b] *Dipartimento di Ingegneria Civile*
Università di Roma "Tor Vergata"
via del Politecnico 1, 00133 Roma, Italy

Abstract

We study an evolutive model for electrical conduction in biological tissues, where the conductive intra-cellular and extracellular spaces are separated by insulating cell membranes. The mathematical scheme is an elliptic problem, with dynamical boundary conditions on the cell membranes. The problem is set in a finely mixed periodic medium. We show that the homogenization limit u_0 of the electric potential, obtained as the period of the microscopic structure approaches zero, solves the equation

$$-\operatorname{div}\left(\sigma_0\nabla_x u_0 + A^0\nabla_x u_0 + \int\limits_0^t A^1(t-\tau)\nabla_x u_0(x,\tau)\,\mathrm{d}\tau - \mathcal{F}(x,t)\right) = 0\,,$$

where $\sigma_0 > 0$ and the matrices A^0, A^1 depend on geometric and material properties, while the vector function $\mathcal{F}$ keeps trace of the initial data of the original problem. Memory effects explicitly appear here, making this elliptic equation of non standard type.

Key words: continuum mechanics, electrical conduction, homogenization, biomathematics

1 Introduction

We consider a model for the electrical conduction in a medium composed of two different conductive phases, separated by a dielectric interface. This physical framework can be applied to electrical conduction in biological tissues, where one of the phases is the extracellular space, the other one is the intra-cellular space, and the interface is the cell membrane. Our model is designed to investigate the response of biological tissues to the injection of electrical currents in the radio-frequency range, that is the Maxwell–Wagner interfacial polarization effect (see [4]). This effect is relevant in clinical applications like electric tomography and body composition (see [3]).

The mathematical scheme consists in partial differential equations of elliptic type prescribed in each phase, complemented with suitable boundary conditions at the interface, and at the boundary of the spatial domain. The unknown function is here the electric potential.

Since the problem evolves in time, we have a family of elliptic problems parametrized by time; but the dependence of the unknown on time is not merely parametrical. Indeed, due to the resistive/capacitive behavior of the interface, the potential jumps across the interface, and the jump satisfies a dynamical condition.

On the other hand, also in view of the applications we have in mind, we assume that the two phases are finely mixed with a microscopic periodic structure, so that the problem contains a small parameter ε, coinciding with the period of the microstructure. We investigate the homogenization limit of the electric potential u_ε when we let $\varepsilon \to 0$, in order to obtain a macroscopic model for the limiting potential u_0.

1.1 Main result

Let Ω be a bounded open connected set of $\boldsymbol{R}^N$, $N \geq 2$. Let $Y = (0,1)^N$, and let $E_1 \subset Y$ be an open set made of a finite number of connected components whose closures do not intersect one another, or ∂Y. We assume that $E_2 = Y \setminus \overline{E_1}$ is a connected set. For each $\varepsilon > 0$, we define the intra-cellular space Ω_1^ε as the part of the periodic lattice $\varepsilon z + \varepsilon E_1$, $z \in \boldsymbol{Z}$, which is compactly contained in Ω. The extracellular space Ω_2^ε is defined as $\Omega \setminus \overline{\Omega_1^\varepsilon}$, and $\Gamma^\varepsilon = \partial \Omega_1^\varepsilon$ will represent the cell membranes. We assume that Γ^ε and $\partial \Omega$ are smooth. Note that $\Gamma^\varepsilon \cap \partial \Omega = \varnothing$, and that Ω_2^ε is connected, so that we are in the setting of [5].

We look at the homogenization limit as $\varepsilon \to 0$ of the problem for $u_\varepsilon(x,t)$ (here

the operators div and ∇ act only with respect to the space variable x)

$$- \operatorname{div}(\sigma_1 \nabla u_\varepsilon) = 0 , \qquad\qquad \text{in } \Omega_1^\varepsilon; \qquad\qquad (1.1)$$
$$- \operatorname{div}(\sigma_2 \nabla u_\varepsilon) = 0 , \qquad\qquad \text{in } \Omega_2^\varepsilon; \qquad\qquad (1.2)$$
$$\sigma_1 \nabla u_\varepsilon^{(\mathrm{int})} \cdot \nu = \sigma_2 \nabla u_\varepsilon^{(\mathrm{out})} \cdot \nu , \qquad \text{on } \Gamma^\varepsilon; \qquad\qquad (1.3)$$
$$\frac{\alpha}{\varepsilon} \frac{\partial}{\partial t}[u_\varepsilon] + \frac{\beta}{\varepsilon}[u_\varepsilon] = \sigma_2 \nabla u_\varepsilon^{(\mathrm{out})} \cdot \nu , \qquad \text{on } \Gamma^\varepsilon; \qquad\qquad (1.4)$$
$$[u_\varepsilon](x,0) = S_\varepsilon(x) , \qquad\qquad \text{on } \Gamma^\varepsilon; \qquad\qquad (1.5)$$
$$u_\varepsilon(x,t) = 0 , \qquad\qquad \text{on } \partial\Omega. \qquad\qquad (1.6)$$

The notation in (1.1)–(1.4), (1.6), means that the indicated equations are in force in the relevant spatial domain for $0 < t < T$. Here σ_1, σ_2, $\alpha > 0$ and $\beta \geq 0$ are constants, and ν is the normal unit vector to Γ^ε pointing into Ω_2^ε. Since u_ε is not in general continuous across Γ^ε we have set

$$u_\varepsilon^{(\mathrm{int})} := \text{ trace of } u_{\varepsilon|\Omega_1^\varepsilon} \text{ on } \Gamma^\varepsilon; \quad u_\varepsilon^{(\mathrm{out})} := \text{ trace of } u_{\varepsilon|\Omega_2^\varepsilon} \text{ on } \Gamma^\varepsilon.$$

We also denote

$$[u_\varepsilon] := u_\varepsilon^{(\mathrm{out})} - u_\varepsilon^{(\mathrm{int})} .$$

Similar conventions are employed for other quantities; we also set

$$\sigma = \sigma_1 \quad \text{in } \Omega_1^\varepsilon, \qquad \sigma = \sigma_2 \quad \text{in } \Omega_2^\varepsilon.$$

The initial data S_ε satisfies

$$S_\varepsilon(x) = \varepsilon S_1\left(x, \frac{x}{\varepsilon}\right) + \varepsilon^2 S_2\left(x, \frac{x}{\varepsilon}\right) + o(\varepsilon^2) ,$$

where $\|S_1\|_\infty$, $\|S_2\|_\infty < \infty$, $S_1(x,y)$, $S_2(x,y)$ are continuous in x, uniformly with respect to $y \in \partial E_1 \pmod{\mathbf{Z}}$, and Y-periodic in y, for all $x \in \Omega$. The dependence of S_1, S_2 on the variable $y = x/\varepsilon$ is introduced in order to take fully into account the effect of the microscopic structure in the homogenized problem.

Here $u_{\varepsilon|\Omega_i^\varepsilon} \in H^1(\Omega_i^\varepsilon)$, and (1.1)–(1.6) are solved in a standard weak sense.

For the sake of simplicity we have taken zero Dirichlet data in (1.6), but more realistic nonhomogeneous data are treated with the same approach, leading to the same limiting equation (see [1]).

Theorem 1 *Under the previous assumptions, $u_\varepsilon \to u_0$ weakly in $L^2(\Omega)$ as $\varepsilon \to 0$, and the limiting potential $u_0 \in H^1_o(\Omega)$ solves in the sense of distributions the equation*

$$- \operatorname{div}\left(\sigma_0 \nabla_x u_0 + A^0 \nabla_x u_0 + \int_0^t A^1(t-\tau)\nabla_x u_0(x,\tau)\,\mathrm{d}\tau - \mathcal{F}(x,t)\right) = 0 \quad (1.7)$$

where the matrices A^0, A^1 and the vector function $\mathcal{F}$ are defined in (2.34), (2.35), and $\sigma_0 > 0$ is defined in (2.23).

In next Section in order to identify the limit function, we make use of the Laplace transform (see [7]). More precisely, we first obtain the limit equation of the Laplace transform of problem (1.1)–(1.6), which gives a stationary scheme resembling a scheme studied by [5] in the context of linear elasticity. Then, we achieve the homogenized equation (1.7), applying the inverse Laplace transform to the stationary limit equation.

2   Derivation of the homogenized equation

Multiplying (1.1), (1.2) by u_ε and integrating by parts we arrive for all $0 < t < T$ to the energy estimate

$$\int\limits_0^t\!\!\int\limits_\Omega \sigma |\nabla u_\varepsilon|^2 \,\mathrm{d}x\,\mathrm{d}\tau + \frac{\alpha}{2\varepsilon}\int\limits_{\Gamma^\varepsilon} [u_\varepsilon]^2(x,t)\,\mathrm{d}\sigma + \frac{\beta}{\varepsilon}\int\limits_0^t\!\!\int\limits_{\Gamma^\varepsilon} [u_\varepsilon]^2 \,\mathrm{d}\sigma\,\mathrm{d}\tau = \frac{\alpha}{2\varepsilon}\int\limits_{\Gamma^\varepsilon} S_\varepsilon^2(x)\,\mathrm{d}\sigma\,.$$

$$(2.1)$$

Since $|\Gamma^\varepsilon|_{N-1} \sim 1/\varepsilon$, the right hand side of (2.1) is stable as $\varepsilon \to 0$ if $S_\varepsilon = O(\varepsilon)$, motivating our assumptions on S_ε. This uniform estimate, together with a Poincaré-type inequality for functions with jumps (see [5], [1]) yield an uniform L^2 bound for u_ε, which in turn implies weak L^2 convergence of a subsequence of u_ε to a limit u_0; in the following we still denote such a subsequence by u_ε.

One may check that the Laplace transforms

$$U_\varepsilon(x,s) = \int\limits_0^\infty e^{-st} u_\varepsilon(x,t)\,\mathrm{d}t\,,$$

are well defined for $s \in \boldsymbol{C}$, where $\mathrm{Re}\,(s)$ is assumed to be large enough, and that the U_ε converge weakly to

$$\widetilde{U}_0(x,s) = \int\limits_0^\infty e^{-st} u_0(x,t)\,\mathrm{d}t\,. \qquad (2.2)$$

As customary when employing Laplace transforms, we assume that u_ε and all other functions depending on t identically vanish for $t < 0$. Let us calculate

$$\int\limits_0^\infty e^{-st} \frac{\partial}{\partial t}[u_\varepsilon]\,\mathrm{d}t = -S_\varepsilon(x) + s[U_\varepsilon]\,.$$

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Then the problem solved by U_ε is

$$-\operatorname{div}(\sigma\nabla U_\varepsilon)=0\,, \qquad\qquad \text{in } \Omega_1^\varepsilon,\ \Omega_2^\varepsilon; \qquad (2.3)$$

$$[\sigma\nabla U_\varepsilon\cdot\nu]=0\,, \qquad\qquad \text{on } \Gamma^\varepsilon; \qquad (2.4)$$

$$\frac{\tilde\alpha}{\varepsilon}[U_\varepsilon]=\frac{\alpha}{\varepsilon}S_\varepsilon(x)+\sigma_2\nabla U_\varepsilon^{(\text{out})}\cdot\nu\,, \qquad \text{on } \Gamma^\varepsilon; \qquad (2.5)$$

$$U_\varepsilon(x,t)=0\,, \qquad\qquad \text{on } \partial\Omega, \qquad (2.6)$$

where $\tilde\alpha=\tilde\alpha(s)=\alpha s+\beta$.

Existence of solutions to this problem follows from a standard application of Lax-Milgram theorem; the same applies to the cell problems stated below.

In order to identify the limiting problem we apply the classical two-scale approach (see [2]), and consider the asymptotic expansion in powers of ε

$$U_\varepsilon(x,s)=U_0(x,y,s)+\varepsilon U_1(x,y,s)+\varepsilon^2 U_2(x,y,s)+\dots\,,$$

where $y=x/\varepsilon$ is the microscopic variable. Here U_0, U_1 and U_2 are periodic in $y\in Y$, and U_1, U_2 have zero integral average over Y. Then

$$\nabla U_\varepsilon=\frac{1}{\varepsilon}\nabla_y U_0+\left(\nabla_x U_0+\nabla_y U_1\right)+\varepsilon\left(\nabla_x U_1+\nabla_y U_2\right)+\dots\,.$$

A similar decomposition of ΔU_ε can be easily found. On substituting these expansions in the problem (2.3)–(2.6), one finds the boundary problems solved by U_0, U_1 and U_2 in the period cell Y. The term U_0 satisfies

$$-\sigma\,\Delta_y U_0=0\,, \qquad\qquad \text{in } E_1,\ E_2; \qquad (2.7)$$

$$[\sigma\nabla_y U_0\cdot\nu]=0\,, \qquad\qquad \text{on } \Gamma; \qquad (2.8)$$

$$\tilde\alpha[U_0]=\sigma_2\nabla_y U_0^{(\text{out})}\cdot\nu\,, \qquad \text{on } \Gamma. \qquad (2.9)$$

As a consequence, $U_0=U_0(x,s)$, a piece of information which we use below; in particular we stress that $[U_0]=0$. Next, we look at U_1, solving

$$-\sigma\,\Delta_y U_1=0\,, \qquad\qquad \text{in } E_1,\ E_2; \qquad (2.10)$$

$$[\sigma\nabla_y U_1\cdot\nu]=-[\sigma\nabla_x U_0\cdot\nu]\,, \qquad \text{on } \Gamma; \qquad (2.11)$$

$$\tilde\alpha[U_1]=\alpha S_1+\sigma_2\nabla_y U_1^{(\text{out})}\cdot\nu+\sigma_2\nabla_x U_0\cdot\nu\,, \qquad \text{on } \Gamma. \qquad (2.12)$$

It is convenient to separate in U_1 the contributions of U_0 and of the initial data S_1; i.e., we write

$$U_1(x,y,s)=-\mathcal{X}(y,s)\cdot\nabla_x U_0(x,s)+\mathcal{S}(x,y,s)\,.$$

Here the (transformed) cell functions $\mathcal{X}_h$ satisfy for $h = 1, \ldots, N$,

$$-\sigma \, \Delta_y \, \mathcal{X}_h = 0 \,, \qquad\qquad \text{in } E_1, \, E_2; \qquad (2.13)$$

$$[\sigma(\nabla_y \mathcal{X}_h - \boldsymbol{e}_h) \cdot \nu] = 0 \,, \qquad\qquad \text{on } \Gamma; \qquad (2.14)$$

$$\tilde{\alpha}[\mathcal{X}_h] = \sigma_2(\nabla_y \mathcal{X}_h^{(\mathrm{out})} - \boldsymbol{e}_h) \cdot \nu \,, \qquad \text{on } \Gamma, \qquad (2.15)$$

where $\{\boldsymbol{e}_h\}$ is the standard basis in $\boldsymbol{R}^N$. As usual, the $\mathcal{X}_h$ are assumed: i) to be periodic in Y; ii) to have zero integral average over Y. Moreover $\mathcal{S}$, besides fulfilling requirements i) and ii), must satisfy

$$-\sigma \, \Delta_y \, \mathcal{S} = 0 \,, \qquad\qquad \text{in } E_1, \, E_2; \qquad (2.16)$$

$$[\sigma \nabla_y \mathcal{S} \cdot \nu] = 0 \,, \qquad\qquad \text{on } \Gamma; \qquad (2.17)$$

$$\tilde{\alpha}[\mathcal{S}] = \alpha S_1(x, y) + \sigma_2 \nabla_y \mathcal{S}^{(\mathrm{out})} \cdot \nu \,, \qquad \text{on } \Gamma. \qquad (2.18)$$

The limiting equation will be obtained as a compatibility condition necessary for the solvability of the problem for U_2

$$-\sigma \, \Delta_y \, U_2 = \sigma \, \Delta_x \, U_0 + 2\sigma \frac{\partial^2 U_1}{\partial x_j \partial y_j} \,, \qquad\qquad \text{in } E_1, \, E_2; \qquad (2.19)$$

$$[\sigma \nabla_y U_2 \cdot \nu] = -[\sigma \nabla_x U_1 \cdot \nu] \,, \qquad\qquad \text{on } \Gamma; \qquad (2.20)$$

$$\tilde{\alpha}[U_2] = \alpha S_2 + \sigma_2 \nabla_y U_2^{(\mathrm{out})} \cdot \nu + \sigma_2 \nabla_x U_1^{(\mathrm{out})} \cdot \nu \,, \qquad \text{on } \Gamma. \qquad (2.21)$$

Indeed, after straightforward calculations, we arrive at

$$\sigma_0 \, \Delta_x \, U_0 = \int_Y \sigma \, \Delta_x \, U_0 \, \mathrm{d}y = \int_\Gamma [\sigma \nabla_x U_1 \cdot \nu] \, \mathrm{d}\sigma$$

$$= \mathrm{div} \left(-\int_\Gamma \nu \otimes [\sigma \mathcal{X}] \, \mathrm{d}\sigma \, \nabla_x U_0 + \int_\Gamma [\sigma \mathcal{S}] \nu \, \mathrm{d}\sigma \right), \quad (2.22)$$

where

$$\sigma_0 = |E_1|\sigma_1 + |E_2|\sigma_2 \,, \qquad (2.23)$$

and $\otimes$ denotes the standard tensor product.

We can prove that for large enough $\mathrm{Re}\, s$, equation (2.22), complemented with homogeneous Dirichlet boundary conditions, has a unique solution $U_0 \in H_o^1(\Omega)$, which is holomorphic in s. For $s \in \boldsymbol{R}$ problem (2.3)–(2.6) is similar to the one of [5]. However, the inhomogeneous term in (2.5), due to the initial data S_ε and leading to the source term in (2.22), was not present there. It is possible, anyway, to apply the techniques of [5] to obtain that, for $s \in \boldsymbol{R}$, the sequence $\{U_\varepsilon\}$ converges to the function U_0. Hence, by unique holomorphic extension, we conclude that $U_0 = \tilde{U}_0$, where $\tilde{U}_0$ has been defined in (2.2), and that the whole sequence U_ε converges to U_0.

In order to obtain the limiting equation in the variable space (x,t), it is only left to anti-transform (2.22); this is best done by splitting

$$\mathcal{X}(y,s) = \chi^0(y) + \mathcal{X}^1(y,s),$$

where

$$-\sigma\,\Delta_y\,\chi_h^0 = 0\,, \qquad \text{in } E_1,\, E_2; \qquad (2.24)$$
$$[\sigma(\nabla_y\chi_h^0 - e_h)\cdot\nu] = 0\,, \qquad \text{on } \Gamma; \qquad (2.25)$$
$$[\chi_h^0] = 0\,, \qquad \text{on } \Gamma. \qquad (2.26)$$

Moreover

$$-\sigma\,\Delta_y\,\mathcal{X}_h^1 = 0\,, \qquad\qquad\qquad \text{in } E_1,\, E_2; \quad (2.27)$$
$$[\sigma\nabla_y\mathcal{X}_h^1\cdot\nu] = 0\,, \qquad\qquad\qquad \text{on } \Gamma; \quad (2.28)$$
$$\tilde{\alpha}[\mathcal{X}_h^1] = \sigma_2(\nabla_y\chi_h^{0\,\text{(out)}} - e_h)\cdot\nu + \sigma_2\nabla_y\mathcal{X}_h^{1\,\text{(out)}}\cdot\nu\,, \quad \text{on } \Gamma. \quad (2.29)$$

Denote by $\mathcal{L}^{-1}$ the inverse Laplace transform. We have

$$\mathcal{L}^{-1}\left(\int_\Gamma \nu\otimes[\sigma\mathcal{X}^1](y,s)\,\mathrm{d}\sigma\,\nabla_x U_0(x,s)\right)$$
$$= \int_0^t \left\{\int_\Gamma \nu\otimes[\sigma\mathcal{L}^{-1}(\mathcal{X}^1)](y,t-\tau)\,\mathrm{d}\sigma\right\}\nabla_x u_0(x,\tau)\,\mathrm{d}\tau\,.$$

Note that the existence of the inverse Laplace transforms appearing above follows from standard estimates of $\mathcal{X}^1$ (a similar remark applies to $\mathcal{L}^{-1}(\mathcal{S})$ below). Define $\chi^1 = \mathcal{L}^{-1}(\mathcal{X}^1)$; then it can be easily checked that

$$\alpha[\chi_h^1(y,0)] = \sigma_2(\nabla_y\chi_h^{0\,\text{(out)}} - e_h)\cdot\nu\,,$$
$$\chi_h^1 = \mathcal{T}([\chi_h^1(\cdot,0)])\,.$$

Here the transform $\mathcal{T}(g)$ is defined by $\mathcal{T}(g) = v$, where v is the solution to

$$-\sigma\,\Delta_y\,v = 0\,, \qquad\qquad \text{in } E_1,\, E_2; \qquad (2.30)$$
$$[\sigma\nabla_y v\cdot\nu] = 0\,, \qquad\qquad \text{on } \Gamma; \qquad (2.31)$$
$$\alpha\frac{\partial}{\partial t}[v] + \beta[v] = \sigma_2\nabla_y v^{\text{(out)}}\cdot\nu\,, \qquad \text{on } \Gamma; \qquad (2.32)$$
$$[v](y,0) = g(y)\,, \qquad\qquad \text{on } \Gamma; \qquad (2.33)$$

here v is a periodic function in Y, such that $\int_Y v\,\mathrm{d}y = 0$. The problem (2.30)–(2.33) is parabolic in the abstract sense of [6], chapter 7.

By means of similar reasoning, one finds that

$$\mathcal{L}^{-1}(\mathcal{S}(x,\cdot,\cdot)) = \mathcal{T}(S_1(x,\cdot))\,.$$

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Therefore u_0 solves (1.7), where the matrices A^0 and A^1 are defined by

$$A^0 = \int_\Gamma \nu \otimes [\sigma]\chi^0 \, d\sigma \,, \qquad A^1(t) = \int_\Gamma \nu \otimes [\sigma\chi^1](t) \, d\sigma \,, \qquad (2.34)$$

and

$$\mathcal{F}(x,t) = \int_\Gamma [\sigma\mathcal{T}(S_1(x,\cdot))](y,t)\nu \, d\sigma \,. \qquad (2.35)$$

The matrices A^0 and A^1 are symmetric, and $\sigma_0 I + A^0$ is positive definite (see [1]).

3   Remarks on the $\mathcal{T}$ transform

The $\mathcal{T}$ transform can be rewritten in a more expressive way by introducing the operator

$$\mathcal{C}(g) = -\sigma_2 \nabla v^{(\text{out})} \cdot \nu \,,$$

where v solves the elliptic problem (2.30), (2.31), complemented with $[v](y) = g(y)$ on Γ, and is periodic in Y, with zero average there. $\mathcal{C}$ is self-adjoint in $H^{1/2}(\Gamma)$, and $\mathcal{C} + \lambda$ is coercive for $\lambda > 0$ [1]. Let $\{w_n\}$ be a complete orthonormal system of eigenfunctions of $\mathcal{C}$ in $L^2(\Gamma)$, and let $\{\lambda_n\}$ be the corresponding sequence of non negative eigenvalues. It is known (see [6], chapter 7) that

$$[\mathcal{T}(g)](y,t) = \sum_{n=0}^\infty e^{-\frac{\beta+\lambda_n}{\alpha}t} w_n(y) \int_\Gamma g(z)w_n(z) \, d\sigma \,. \qquad (3.1)$$

Indeed, one may formally write (2.32) as

$$\alpha \frac{\partial}{\partial t}[\mathcal{T}(g)] + \beta[\mathcal{T}(g)] = -\mathcal{C}\left([\mathcal{T}(g)]\right) \,.$$

Note that the λ_n, w_n depend only on the geometry of E_1, and on the conductivities σ_1, σ_2. On the other hand, through the representation formula (3.1), the λ_n, w_n enter the homogenized constitutive functions in (1.7). Therefore it is hoped that reconstruction of the constitutive functions in (1.7) may lead to gain some knowledge on the morphology and properties of the biological tissue.

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