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ABOUT THE TRANSMEMBRANE VOLTAGE POTENTIAL OF A BIOLOGICAL CELL IN TIME-HARMONIC REGIME.

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Abstract. The paper presents heuristics to reduce several difficulties related to the determination of the transmembrane voltage potential (TMP) on cells with arbitrary smooth shape. We show how the thin weakly conducting membrane can be replaced by asymptotically equivalent transmission conditions at the interface between the cell interior (the cytoplasm) and the extracellular medium. We describe our formal asymptotic method for constructing precise models of cells. This method is based on an appropriate change of variables in the thin membrane. Our frequency dependent models is helpfull to determine the TMP on cells on which experiment measurements are prohibited. We end the paper by presenting briefly the sketch of the proofs of the asymptotics and the *a priori* error estimates.

Résumé. Dans cet artice, nous présentons une méthode de développement asymptotique de milieu à couche mince en dimension 3 permettant de réduire les difficultés numériques liées au calcul du potentiel transmembranaire d'une cellule biologique. Nous montrons comment la fine membrane faiblement conductrice de la cellule peut être remplacée par des conditions de transmission appropriées sur le bord du cytoplasme. Notre méthode est basée sur un changement de variables adéquat dans la couche mince. Nous obtenons trois différents modèles permettant de décrire le comportement du potentiel quasi-élecrostatique d'un cellule suivant trois types de fréquences: basse, moyenne ou haute fréquences. Ces modèles permettent le calcul du potentiel transmembranaire dans des cellules sur lesquelles des mesures expérimentales sont difficiles à réaliser. Nous concluons en présentant brièvement les principes de démonstration des résultats.

1. Introduction

The distribution of the electromagnetic field in a biological cell is important for bio-electromagnetic investigations. For instance, a sufficiently large amplitude of the transmembranar potential (TMP), which is the difference of the electric potentials between both sides of the cell membrane, leads to an increase of the membrane permeability [12,17]. This phenomenon, called electropermeabilization, has been already used in oncology and holds promises in gene therapy [6, 15], justifying precise assessments of the TMP. Since the experimental measurements of the TMP on living cells are limited — essentially due to the thinness of the cell membrane, which is a few nanometers thick — a numerical approach is often chosen [12,14]. However, these computations are confronted with the heterogeneous parameters of the biological cells.

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1.1. **The electric model of the cell**

In the Schwan model [4, 5], the cell is a medium of smooth shape (without any corner) composed by a homogeneous conducting cytoplasm of diameter of a few micrometers surrounded by a very insulating membrane a few nanometers thick (see Figure 1).

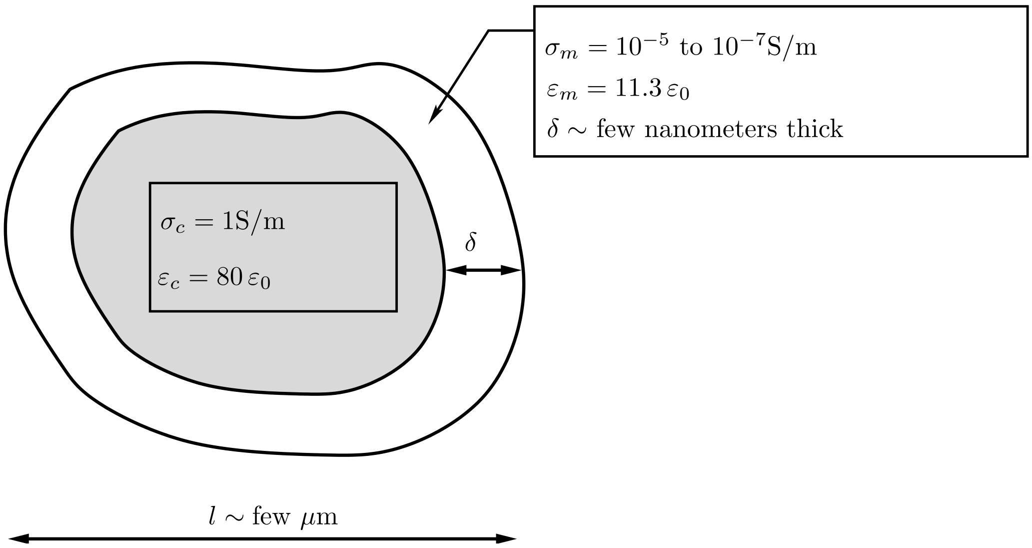

FIGURE 1. The electric model of the biological cell given by Schwan [4].

To avoid difficulties, most of the numerical computations deal with unrealistic cells (spherical and ellipsoidal cells) without details about the accuracy of the numerical method used (typically the finite element method) [4]. However, biological cells have non-trivial shapes and Sebastián *et al.* show in [7, 14] that the cell geometry has a significant influence on the electric field distribution. To perform computations on realistic cell shapes by considering the conduction problem[1], Pucihar *et al.* [12] propose to replace the membrane by an equivalent condition on the boundary of the cytoplasm. This condition corresponds to a contact resistance model but the details for asserting the accuracy of their method are not given.

In this paper we consider the realistic threedimensional model of biological cell given by Schwan for different frequency ranges. We study the quasi-electrostatic approximation[2] of the electric field. This approximation is usually considered to describe the behavior of a cell submitted to an electric field of frequency smaller than few giga Hertz.

We present a rigorous asymptotic method to replace the thin membrane by an asymptotically equivalent transmission conditions. This method, which leads to precise *a priori* error estimates was extensively presented in previous papers [9–11] in a bidimensional domain. It is based on an appropriate change of variables in the thin layer in order to make appear the small parameter (the thickness of the membrane) in the equations satisfied by the electric potential.

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[1]The conduction problem consists of dealing with the steady-state voltage potentials or in other words the electrostatic field.

[2]The quasi-electrostatic approximation consists of neglecting the curl part of the electric field, which therefore derives from a potential so-called quasi-electrostatic voltage potential. This amounts to considering the steady state voltage potential equations with complex coefficients.

Denote by z_c and z_m the respective complex permittivities of the cytoplasm and of the membrane defined as functions of the pulsation[3] by:

$$\forall \omega \geq 0, \quad z_c(\omega) = \mathrm{i}\omega\varepsilon_c + \sigma_c, \quad z_m(\omega) = \mathrm{i}\omega\varepsilon_m + \sigma_m,$$

where $(\varepsilon_c, \sigma_c)$ and $(\varepsilon_m, \sigma_m)$ are the respective dielectric properties of the cytoplasm and of the membrane given in Fig. 1. According to these properties, and unlike the domains considered in [10, 11], the cell is a highly heterogeneous medium for pulsations smaller than 10^8rad/s, since $|z_m(\omega)/z_c(\omega)| \leq 10^{-2}$, while it is a heterogeneous medium for frequencies greater than 100 MHz, since $|z_m(\omega)/z_c(\omega)| \sim 10^{-1}$. Therefore the asymptotics of [10, 11] may be used only at "high" frequency, meaning for frequencies such that the cell is not highly heterogeneous. Actually the relative thickness of the membrane is of order 10^{-3}, *i.e.* of the same order as the ratio $|z_m(\omega)/z_c(\omega)|$ for low frequencies (δ is even much greater than $|z_m(\omega)/z_c(\omega)|$ for frequencies smaller than 10KHz). It is therefore necessary to take into account the highly heterogeneous character of the cell in the equations instead of considering that the moduli of the involved complex permittivities are of order 1, as in [10, 11]. The aim of this paper is to replace the thin membrane by equivalent conditions on the boundary of the cytoplasm for realistic complex permittivities of the cell components. With these conditions the thin membrane does not have to be meshed, and therefore more accurate and more efficient numerical simulations may be performed.

1.2. **Statement of the problem**

Let δ be a small positive number without physical dimension and representing the thickness of the membrane. Let Ω be a smooth bounded domain of $\mathbb{R}^3$ composed by three domains: the cytoplasm $\mathcal{O}_c$, which is a smooth bounded domain with connected compact and orientable boundary, the cell membrane $\mathcal{O}_m^\delta$ of thickness δ, which surrounds $\mathcal{O}_c$ and the extracellular matrix $\mathcal{O}_e^\delta$. We suppose that the electric properties $(\varepsilon_e, \sigma_e)$ of the extracellular matrix are similar to these of cytoplasm (but not necessary exactly the same). Similarly to z_c (and z_m) we denote by z_e the complex permittivity of the ambient medium defined by:

$$\forall \omega \geq 0, \quad z_e(\omega) = \mathrm{i}\omega\varepsilon_e + \sigma_e.$$

The geometric and electromagnetic considered data are summarized in Fig. 2. To perform our asymptotic expansion, we have to consider adimensionalized quantities. We refer the reader to [8] for a precise description of the adimensionalization. We denote by z the adimensionalized complex permittivity of Ω defined by:

$$\forall \omega \geq 0, \forall x \in \Omega, \quad z(\omega, x) = \begin{cases} z_c(\omega), \text{ if } x \in \mathcal{O}_c, \\ z_m(\omega), \text{ if } x \in \mathcal{O}_m^\delta, \\ z_e(\omega), \text{ if } x \in \mathcal{O}_e^\delta. \end{cases}$$

1.2.a. *The quasi-electrostatic formulation*

Let ϕ be a given function in $H^{1/2+s}(\partial\Omega)$, for $s \geq 0$. The quasi-electrostatic potential u^δ at the frequency $\omega/2\pi$ satisfied the well-known elliptic problem in Ω:

$$\nabla.\left(z(\omega, .)\nabla u^\delta\right) = 0, \text{ in } \Omega, \tag{1a}$$

$$u^\delta|_{\partial\Omega} = \phi, \text{ in } \partial\Omega. \tag{1b}$$

[3]Remember that the pulsation ω is linked to the frequency f by the equality :

$$\omega = 2\pi f.$$

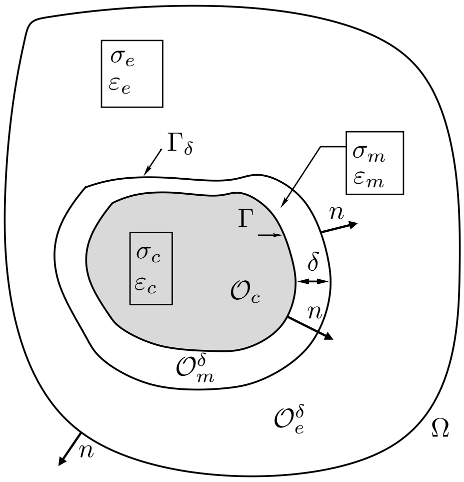

FIGURE 2. Geometric and dielectric data [4].

We are interested in approaching the exact potential u^δ by an approximated potential u_{app} such that for a certain norm, which will be made precise later on, the following estimate holds:

$$\|u^\delta - u_{app}\| \leq C\delta^2,$$

for a δ–independent constant C. As we said above, since the cell may be highly heterogeneous for several frequencies, it is necessary to make appear explicitly the small (adimensionalized) parameter δ in the expression of $z(\omega, .)$. This is the reason why we choose five pulsations

$$\omega_{LF} \leq \omega_{MF}^- \leq \omega_{MF}^+ \leq \omega_{HF}^- \leq \omega_{HF}^+,$$

which permit to define our three frequency regimes respectively called low frequency, mid-frequency and high frequency.

1.2.b. *The low frequency range*

The low frequency range corresponds to pulsations ω such that $0 \leq \omega \leq \omega_{LF}$. For these frequencies, we suppose there exists three constants β_e, β_c and β_m of order 1 and three functions of ω denoted by α_e, α_m and α_c such that

$$\begin{aligned} z_e(\omega) &= \beta_e + \mathrm{i}\delta^2\alpha_e(\omega), \\ z_c(\omega) &= \beta_c + \mathrm{i}\delta^2\alpha_c(\omega), \\ z_m(\omega) &= \delta^2\left(\beta_m + \mathrm{i}\alpha_m(\omega)\right). \end{aligned}$$

Moreover we suppose there exists a δ–independant constant $c > 0$ such that:

$$\forall 0 \leq \omega \leq \omega_{LF}, \quad \begin{cases} |\alpha_e(\omega)| \leq c, \\ |\alpha_c(\omega)| \leq c, \\ |\alpha_m(\omega)| \leq c. \end{cases}$$

1.2.c. *The mid-frequency range*

The mid-frequency range corresponds to pulsations ω satisfying $\omega^-_{MF} \;\leq\; \omega \;\leq\; \omega^+_{MF}$. Similarly to the low frequency range we suppose there exists three functions α_e, α_m and α_c such that

$$\begin{aligned} z_e(\omega) &= \beta_e + \mathrm{i}\delta\alpha_e(\omega), \\ z_c(\omega) &= \beta_c + \mathrm{i}\delta\alpha_c(\omega), \\ z_m(\omega) &= \delta^2\beta_m + \mathrm{i}\delta\alpha_m(\omega). \end{aligned}$$

The functions α_e, α_c and α_m are defined such that there exists δ–independant constants $C > 0$ and $c > 0$ such that:

$$\forall \omega^-_{MF} \;\leq\; \omega \;\leq\; \omega^+_{MF}, \quad \begin{cases} c \leq |\alpha_e(\omega)| \leq C, \\ c \leq |\alpha_c(\omega)| \leq C, \\ c \leq |\alpha_m(\omega)| \leq C. \end{cases}$$

1.2.d. *The high frequency range*

The high frequency regime corresponds to pulsations ω such that $\omega^-_{HF} \;\leq\; \omega \;\leq\; \omega^+_{HF}$, such that

$$\begin{aligned} z_e &= \beta_e + \mathrm{i}\alpha_e(\omega), \\ z_c &= \beta_c + \mathrm{i}\alpha_c(\omega), \\ z_m &= \delta^2\beta_m + \mathrm{i}\alpha_m(\omega), \end{aligned}$$

where α_e, α_c and α_m satisfies the following inequalities, for $C > 0$ and $c > 0$:

$$\forall \omega^-_{HF} \;\leq\; \omega \;\leq\; \omega^+_{HF}, \quad \begin{cases} c \leq |\alpha_e(\omega)| \leq C, \\ c \leq |\alpha_c(\omega)| \leq C, \\ c \leq |\alpha_m(\omega)| \leq C. \end{cases}$$

Remark 1.1. For biological cells δ equals 1/1000. The definition of our three frequency regimes is quiet subjective, since it is not clear that for example 1/100 may be consider as of order 1 or δ. For instance consider that a given quantity a is of order 1 if $0.1 \leq a \leq 10$. Such choice leads to the following determination:

$$\begin{aligned} \omega_{LF} &= 10^5, \\ \omega^-_{MF} &= 10^6, \\ \omega^+_{MF} &= 10^8, \\ \omega^-_{HF} &= 10^9, \\ \omega^+_{HF} &= 10^{10}. \end{aligned}$$

Observe this determination does not make precise whether pulsations greater than 10^5 and smaller than 10^6 are either low frequencies or mid-frequencies (and similarly pulsations greater than 10^8 and smaller than 10^9 may be considered as mid-frequencies as well as high frequencies). We leave these appreciations to the scientists of bio-electromagnetic research area.

The most important feature of our modelization lies in the three different expressions of the complex permittivities $(z_e(\omega), z_m(\omega), z_c(\omega))$ in terms of δ. Our following results point out the fact that these three expressions lead to completely different asymptotic transmission conditions.

1.3. **Main results**

Present now our main results. We denote by Γ the smooth (connected compact and orientable) boundary of the cytoplasm. The mean curvature of Γ is denoted by $\mathscr{H}$ and is given explicitly by (12). We define by $u^{e,\delta}$ and $u^{c,\delta}$ the restrictions of u^δ defined by (1) respectively to $\mathcal{O}_e^\delta$ and $\mathcal{O}_c$. Our asymptotic method leads to the definition of u^c_{app} in $\mathcal{O}_c$ and u^e_{app} in $\Omega \setminus \mathcal{O}_c$ for the three different frequency ranges.

1.3.a. *Low frequency approximation*

In order to get the asymptotic expansion of u^δ for low frequencies, we need the following function F defined by:

$$\Delta F = 0, \text{ in } \Omega \setminus \mathcal{O}_c, \tag{2}$$

$$\partial_n F|_\Gamma = 1, \quad F|_{\partial\Omega} = 0. \tag{3}$$

We suppose that the Dirichlet boundary data ϕ of problem (1) satisfies the following equality:

$$\int_{\partial\Omega} \phi(\sigma)\partial_n F(\sigma)\ \mathrm{d}\sigma = 0. \tag{4}$$

Remark 1.2. If (4) is not satisfied, just replace ϕ by

$$\tilde{\phi} = \phi - \frac{\int_{\partial\Omega} \phi(\sigma)F(\sigma)\ \mathrm{d}\sigma}{\int_{\partial\Omega} F(\sigma)\ \mathrm{d}\sigma},$$

and u^δ equals

$$u^\delta = \tilde{u}^\delta + \frac{\int_{\partial\Omega} \phi(\sigma)F(\sigma)\ \mathrm{d}\sigma}{\int_{\partial\Omega} F(\sigma)\ \mathrm{d}\sigma},$$

where $\tilde{u}^\delta$ is the solution to problem (1) with $\tilde{\phi}$ as Dirichlet boundary data.

Then the approximated "low frequency" potentials u^e_{app} and u^c_{app} are respectively defined in $\Omega \setminus \mathcal{O}_c$ and $\mathcal{O}_c$ by

$$\Delta u^e_{app} = 0, \text{ in } \Omega \setminus \mathcal{O}_c, \tag{5a}$$

$$u^e_{app}|_{\partial\Omega} = \phi, \quad \partial_n u^e_{app}|_{\Gamma^+} = \delta \frac{\beta_m + \mathrm{i}\alpha_m(\omega)}{\beta_e} u^e_{app}|_{\Gamma^+} + \delta\Delta|_\Gamma u^e_{app}|_{\Gamma^+}, \tag{5b}$$

and u^c_{app} is defined by

$$\Delta u^c_{app} = 0, \text{ in } \mathcal{O}_c, \tag{6a}$$

$$\partial_n u^c_{app}|_{\Gamma^-} = \delta \frac{\beta_m + \mathrm{i}\alpha_m(\omega)}{\beta_c} u^e_{app}|_{\Gamma^+} \tag{6b}$$

with the Gauge condition

$$\int_\Gamma \left(1 + \delta\left(\mathscr{H}(\sigma) + \frac{(\beta_m + \mathrm{i}\alpha_m(\omega))}{\beta_e}\right)\right) u^c_{app}(\sigma)F(\sigma)\ \mathrm{d}\sigma = \int_\Gamma \left(1 + \delta\left(\mathscr{H}(\sigma) + \frac{(\beta_m + \mathrm{i}\alpha_m(\omega))}{\beta_e}\right)\right) u^e_{app}(\sigma)F(\sigma)\ \mathrm{d}\sigma. \tag{6c}$$

1.3.b. *Mid-frequency approximation*

For mid-frequencies we define the respective approximated potentials u^e_{app} and u^c_{app} in $\Omega \setminus \mathcal{O}_c$ and $\mathcal{O}_c$ by

$$\begin{cases} \Delta u^e_{app} = 0, \text{ in } \mathcal{O}_e, \\ \Delta u^c_{app} = 0, \text{ in } \Omega \setminus \mathcal{O}_e, \\ u^e_{app}\big|_{\partial\Omega} = \phi, \end{cases} \tag{7a}$$

with the transmission conditions

$$\beta_c \partial_n u^c_{app}|_{\Gamma^-} - \beta_e \partial_n u^e_{app}|_{\Gamma^+} = \delta \mathrm{i} \left(\frac{\alpha_e(\omega)}{\beta_c} - \alpha_c(\omega) \right) \partial_n u^c_{app}|_{\Gamma^-} - \delta \beta_e \Delta|_\Gamma u^e_{app}|_{\Gamma^+}, \tag{7b}$$

$$u^c_{app}|_{\Gamma^-} - u^e_{app}|_{\Gamma^+} = \frac{\mathrm{i}\beta_e}{\alpha_m(\omega)} \partial_n u^e_{app}|_{\Gamma^+} + \delta \left(1 + \mathrm{i}\mathscr{H} \frac{\beta_e}{\alpha_m(\omega)} \right) \partial_n u^e_{app}|_{\Gamma^+}. \tag{7c}$$

1.3.c. *High frequency approximation*

We define the respective approximated "high frequency" potentials u^e_{app} and u^c_{app} in $\Omega \setminus \mathcal{O}_c$ and $\mathcal{O}_c$ by

$$\begin{cases} \Delta u^e_{app} = 0, \text{ in } \mathcal{O}_e, \\ \Delta u^c_{app} = 0, \text{ in } \Omega \setminus \mathcal{O}_e, \\ u^e_{app}\big|_{\partial\Omega} = \phi, \end{cases} \tag{8a}$$

with the transmission conditions

$$z_c(\omega) \partial_n u^c_{app}|_{\Gamma^-} - z_e(\omega) \partial_n u^e_{app}|_{\Gamma^+} = \delta (z_e(\omega) - \mathrm{i}\alpha_m(\omega)) \Delta|_\Gamma u^e_{app}|_{\Gamma^+}, \tag{8b}$$

$$u^c_{app}|_{\Gamma^-} - u^e_{app}|_{\Gamma^+} = \delta \frac{z_e(\omega) - \mathrm{i}\alpha_m(\omega)}{\mathrm{i}\alpha_m(\omega)} \partial_n u^e_{app}|_{\Gamma^+}. \tag{8c}$$

1.3.d. *A priori error estimates*

Theorem 1.3. *Let ω belong to one of the above three frequency regimes. There exists $\delta_0 > 0$ such that for all $\delta \in (0, \delta_0)$, the above potentials u^e_{app} and u^c_{app} exist and are unique.*

Moreover there exists a δ–independent constant $C > 0$ satisfying,

$$\|u^{c,\delta} - u^c_{app}\|_{H^1(\mathcal{O}_c)} \leq C\delta^2,$$

and for any domain Υ compactly embedded in $\Omega \setminus \overline{\mathcal{O}_c}$ there exists $d_0 > 0$ and a δ–independent constant $C > 0$ satisfying, for all $\delta \in (0, d_0)$,

$$\|u^{e,\delta} - u^e_{app}\|_{H^1(\Upsilon)} \leq C\delta^2.$$

The high frequency case, which corresponds to non-highly heterogeneous domains, was treated in [8–10], therefore we refer the reader to these papers for a precise description of the asymptotic method. We focus here on the low and mid-frequency approximations for a threedimensional cell.

Remark 1.4. Observe that if we neglect the terms of δ in the mid-frequency approximation we obtain the model of Pucihar *et al.* [12]. From our analysis it is possible to obtain the *a priori* error estimates of the potential $u_{Pucihar}$ defined by:

$$\begin{cases} \Delta u_{Pucihar} = 0, \text{ in } \mathcal{O}_e, \\ \Delta u_{Pucihar} = 0, \text{ in } \Omega \setminus \mathcal{O}_e, \\ u_{Pucihar}|_{\partial\Omega} = \phi, \end{cases} \tag{9a}$$

with the transmission conditions

$$\beta_c \partial_n u_{Pucihar}|_{\Gamma^-} - \beta_e \partial_n u_{Pucihar}|_{\Gamma^+} = 0, \tag{9b}$$

$$u_{Pucihar}|_{\Gamma^-} - u_{Pucihar}|_{\Gamma^+} = \frac{\mathrm{i}\beta_e}{\alpha_m(\omega)} \partial_n u_{Pucihar}|_{\Gamma^+}. \tag{9c}$$

Actually there exists $\delta_0 > 0$ and a δ–independent constant $C > 0$ satisfying, for all $\delta \in (0, \delta_0)$,

$$\|u^{c,\delta} - u_{Pucihar}\|_{H^1(\mathcal{O}_c)} \leq C\delta.$$

For any domain Υ compactly embedded in $\Omega \setminus \overline{\mathcal{O}_c}$ there exists $d_0 > 0$ and a δ–independent constant $C > 0$ satisfying, for all $\delta \in (0, d_0)$,

$$\|u^{e,\delta} - u_{Pucihar}\|_{H^1(\Upsilon)} \leq C\delta.$$

Moreover we emphasize that the involved constant C in the *a priori* estimates does not blow up for δ tending to zero.

Remark 1.5. Observe that for low and mid-frequencies the geometry of the cell and more precisely the mean curvature of its surface appears in the approximations. From a given image of a cell we need to reconstruct its smooth boundary and then to compute the mean curvature of this surface. Moreover to perform simulations with finite element method it is necessary to obtain an adapted mesh from the cell image. The so-called levelset methods enable to obtain such accurate meshes (from which we can derive the mean curvature of the surface). We refer to the book of Sethian [16] for a description of level set methods. We also refer to [1] and therein references for the construction of anisotropic adapted mesh from a given set of points.

Present now the heuristics of our asymptotic expansion.

2. Formal Asymptotics for low and mid-frequency ranges

2.1. Geometry

Let (x_1, x_2) be a system of local coordinates on Γ:

$$\Gamma = \{\psi(x_1, x_2)\}.$$

In the (x_1, x_2)–coordinates, we denote by n the normal to Γ defined by:

$$n = \frac{\partial_{x_1}\psi \wedge \partial_{x_2}\psi}{|\partial_{x_1}\psi \wedge \partial_{x_2}\psi|}.$$

For δ small enough, the thin domain $\mathcal{O}_m^\delta$ is a tubular neighborhood of Γ, which may be parameterized by:

$$\mathcal{O}_m^\delta = \Big\{ \Phi(x_1,x_2,x_3) = \psi(x_1,x_2) + x_3\delta n(x_1,x_2), \\ \text{with } \psi(x_1,x_2)\in\Gamma \text{ and } x_3\in[0,1] \Big\}.$$

To simplify notations, we denote by $\Gamma\times[0,1]$ the parameterization of $\mathcal{O}_m^\delta$ in local coordinates. The Euclidean metric of $\mathcal{O}_m^\delta$ written in (x_1,x_2,x_3)–coordinates is given by the following matrix $(g_{ij})_{i,j=1,2,3}$:

$$(g_{ij})_{i,j=1,2,3} = \begin{pmatrix} g_{11} & g_{12} & 0 \\ g_{12} & g_{22} & 0 \\ 0 & 0 & \delta^2 \end{pmatrix},$$

where the coefficients g_{ij}, for $i,j=1,2$ equal

$$g_{ij} = \left\langle \partial_{x_i}\Phi, \partial_{x_j}\Phi \right\rangle,$$

while

$$g_{i3} = g_{3i} = \delta_{i3}, \quad i=1,2,3.$$

Denote by (g^{ij}) the inverse matrix of (g_{ij}), and by g the determinant of (g_{ij}). The (g^{ij}) matrix equals:

$$(g^{ij}) = \begin{pmatrix} g_{22}/g & -g_{12}/g & 0 \\ -g_{12}/g & g_{11}/g & 0 \\ 0 & 0 & 1/\delta^2 \end{pmatrix}.$$

The coefficients g_{ij} might be written in terms of the coefficients of the first and the second fundamental forms of Γ in the basis $(\partial_{x_1}\psi, \partial_{x_2}\psi)$ [2]. Actually, denote by

$$\begin{aligned} \mathscr{E}(x_1,x_2) &= \langle \partial_{x_1}\psi, \partial_{x_1}\psi \rangle, \\ \mathscr{F}(x_1,x_2) &= \langle \partial_{x_1}\psi, \partial_{x_2}\psi \rangle, \\ \mathscr{G}(x_1,x_2) &= \langle \partial_{x_2}\psi, \partial_{x_2}\psi \rangle, \\ \mathrm{e}(x_1,x_2) &= -\langle \partial_{x_1}n, \partial_{x_1}\psi \rangle, \\ \mathrm{f}(x_1,x_2) &= -\langle \partial_{x_1}n, \partial_{x_2}\psi \rangle, \\ \mathrm{g}(x_1,x_2) &= -\langle \partial_{x_2}n, \partial_{x_2}\psi \rangle. \end{aligned}$$

Define the following matrix $(a_{ij})_{i,j=1,2}$ by:

$$\begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix} = \frac{1}{\mathscr{E}\mathscr{G} - \mathscr{F}^2} \begin{pmatrix} \mathscr{G} & -\mathscr{F} \\ -\mathscr{F} & \mathscr{E} \end{pmatrix},$$

the vectors $(\partial_{x_i}n)_{i=1,2}$ are defined with the help of $(a_{ij})_{i,j=1,2}$:

$$\partial_{x_1}n = a_{11}\partial_{x_1}\psi + a_{12}\partial_{x_2}\psi, \tag{10a}$$
$$\partial_{x_2}n = a_{21}\partial_{x_1}\psi + a_{22}\partial_{x_2}\psi. \tag{10b}$$

Let h^{ij} be $\langle \partial_{x_i} n, \partial_{x_j} n \rangle$, for $i, j = 1, 2$:

$$\begin{aligned}
\mathrm{h}^{11} &= a_{11}^2 \mathscr{E} + 2a_{12}a_{11}\mathscr{F} + a_{12}^2\mathscr{G},\\
\mathrm{h}^{22} &= a_{22}^2 \mathscr{E} + 2a_{21}a_{22}\mathscr{F} + a_{21}^2\mathscr{G},\\
\mathrm{h}^{12} &= a_{11}a_{21}\mathscr{E} + (a_{11}a_{22} + a_{12}a_{21})\mathscr{F} + a_{22}a_{12}\mathscr{G}.
\end{aligned}$$

Since $g_{ij} = \langle \partial_{x_i}\Phi, \partial_{x_j}\Phi \rangle$ we therefore have:

$$g_{11}(x_1, x_2, x_3) = \mathscr{E}(x_1, x_2) - 2x_3\mathrm{e}(x_1, x_2) + x_3^2\mathrm{h}^{11}, \tag{11a}$$

$$g_{22}(x_1, x_2, x_3) = \mathscr{G}(x_1, x_2) - 2x_3\mathrm{g}(x_1, x_2) + x_3^2\mathrm{h}^{22}, \tag{11b}$$

$$g_{12} = \mathscr{F} - 2x_3\mathrm{f} + x_3^2\mathrm{h}^{12}. \tag{11c}$$

The mean curvature $\mathscr{H}$ of Γ is defined by :

$$\mathscr{H} = \frac{1}{2}\frac{\mathrm{e}\mathscr{G} + \mathrm{g}\mathscr{E} - 2\mathrm{f}\mathscr{F}}{\mathscr{E}\mathscr{G} - \mathscr{F}^2}, \tag{12}$$

we also denote by $\mathscr{K}$ the Gaussian curvature defined by

$$\mathscr{K} = a_{11}a_{22} - a_{12}a_{21}.$$

Since g equals

$$g = g_{11}g_{22} - (g_{12})^2,$$

according to (11) the mean curvature equals

$$\mathscr{H} = -\frac{1}{2}\left.\frac{\partial_{x_3}(\sqrt{g})}{\sqrt{g}}\right|_{x_3=0}.$$

2.2. Change of coordinates

Let us denote by u^e and u^c respectively the electric potential in $\mathcal{O}_e^\delta$ and in $\mathcal{O}_c$, written in Euclidean coordinates, and by u^m the electric potential in $\mathcal{O}_m^\delta$ in the local coordinates:

$$\begin{aligned}
u^e &= u^\delta, \text{ in } \mathcal{O}_e^\delta,\\
u^c &= u^\delta, \text{ in } \mathcal{O}_c,\\
u^m &= u^\delta \,\mathrm{o}\, \Phi, \text{ in } \Gamma \times [0, 1].
\end{aligned}$$

Laplace-Beltrami operator on functions in the metric $(g_{ij})_{i,j=1,2,3}$ is given by the well-known expression (see [3, 13]):

$$\Delta_g = \frac{1}{\sqrt{g}} \sum_{i,j=1,2,3} \partial_{x_i}\left(\sqrt{g}g^{ij}\partial_{x_j}\right). \tag{13}$$

Moreover Laplace-Beltrami operator on Γ is defined by:

$$\begin{aligned}
\Delta_\Gamma = &\frac{1}{\sqrt{\mathscr{E}\mathscr{G} - \mathscr{F}^2}}\partial_{x_1}\left(\frac{1}{\sqrt{\mathscr{E}\mathscr{G} - \mathscr{F}^2}}\left(\mathscr{G}\partial_{x_1} - \mathscr{F}\partial_{x_2}\right)\right)\\
&+ \frac{1}{\sqrt{\mathscr{E}\mathscr{G} - \mathscr{F}^2}}\partial_{x_2}\left(\frac{1}{\sqrt{\mathscr{E}\mathscr{G} - \mathscr{F}^2}}\left(-\mathscr{F}\partial_{x_1} + \mathscr{E}\partial_{x_2}\right)\right).
\end{aligned}$$

Replacing the expressions (11) of (g_{ij}) in (13), we infer the following equality:

$$\Delta_g = \frac{1}{\delta^2}\partial^2_{x_3} - \frac{2}{\delta}\mathscr{H}\partial_{x_3} + \Delta_\Gamma + \partial_{x_3}\left(\frac{\partial_{x_3}\left(\sqrt{g}\right)}{\sqrt{g}}\right)\Bigg|_{x_3=0}\partial_{x_3} + \delta R_\delta,$$

where R_δ is a second order differential operator in the (x_1, x_2)-variables and first order differential operator in x_3. Moreover there exists $C > 0$ such that for all $u \in \mathcal{C}^\infty\Big((0,1); H^{s+1}(\Gamma)\Big)$, $s \geq -1$:

$$\sup_{x_3\in[0,1]} \|R_\delta u(\cdot, x_3)\|_{H^{s-1}(\Gamma)} \leq C \sup_{x_3\in[0,1]} \|u(\cdot, x_3)\|_{H^{s+1}(\Gamma)}.$$

Therefore, we rewrite Problem (1) as follows:

$$\Delta u^e = 0, \text{ in } \mathcal{O}_e^\delta, \tag{14a}$$

$$\Delta u^c = 0, \text{ in } \mathcal{O}_c, \tag{14b}$$

$$\forall\,(x_1, x_2, x_3) \in \Gamma \times [0, 1],$$

$$\frac{1}{\delta^2}\partial^2_{x_3}u^m - \frac{2}{\delta}\mathscr{H}\partial_{x_3}u^m + \Delta_\Gamma u^m + \delta R_\delta u^m = 0, \tag{14c}$$

with transmission conditions written in local coordinates at $x_3 = 0$:

$$z_c(\omega)\partial_n u^c|_\Gamma \circ \Psi = \frac{z_m(\omega)}{\delta}\partial_{x_3}u^m\Big|_{x_3=0}, \tag{14d}$$

$$u^c|_\Gamma \circ \Psi = u^m|_{x_3=0}, \tag{14e}$$

at $x_3 = 1$:

$$z_e(\omega)\partial_n u^e|_{\Gamma_\delta} \circ \Phi(.,1) = \frac{z_m(\omega)}{\delta}\partial_{x_3}u^m\Big|_{x_3=1}, \tag{14f}$$

$$u^e|_{\Gamma_\delta} \circ \Phi(.,1) = u^m|_{x_3=1}, \tag{14g}$$

and with boundary condition

$$u^e|_{\partial\Omega} = \phi. \tag{14h}$$

Here n denotes the exterior normal to Γ and ∂_n is defined by:

$$\partial_n w|_\Gamma = \nabla w|_\Gamma \cdot n,$$

and on Γ_δ by

$$\partial_n w|_{\Gamma_\delta} = \nabla w|_\Gamma \cdot n_{\Gamma_\delta}.$$

Remark 2.1. The vector n_{Γ_δ} equals n. Actually, the normal n_{Γ_δ} to Γ_δ is defined by:

$$n_{\Gamma_\delta}(x_1, x_2) = \frac{\partial_{x_1}\Phi(x_1, x_2, 1) \wedge \partial_{x_2}\Phi(x_1, x_2, 1)}{|\partial_{x_1}\Phi(x_1, x_2, 1) \wedge \partial_{x_2}\Phi(x_1, x_2, 1)|}.$$

Since

$$\partial_{x_1}\Phi \wedge \partial_{x_2}\Phi\Big|_{x_3=1} = (\partial_{x_1}\Psi + \delta\partial_{x_1}n) \wedge (\partial_{x_2}\Psi + \delta\partial_{x_2}n),$$

using equalities (10) we infer:

$$\partial_{x_1}\Phi \wedge \partial_{x_2}\Phi\Big|_{x_3=1} = \Big(1 + \delta(a_{11} + a_{22}) + \delta^2(a_{11}a_{22} - a_{12}a_{21})\Big)n.$$

Since

$$1 + \delta(a_{11} + a_{22}) + \delta^2(a_{11}a_{22} - a_{12}a_{21}) = 1 - 2\delta\mathscr{H} + \delta^2\mathscr{K} > 0$$

for δ small enough, we infer that $n|_{\Gamma_\delta}$ equals n.

2.3. **Ansatz**

Let us set our ansatz:

$$u^e = u_0^e + \delta u_1^e + \cdots\,, \tag{15a}$$

$$u^c = u_0^c + \delta u_1^c + \cdots\,, \tag{15b}$$

$$u^m = u_0^m + \delta u_1^m + \delta^2 u_2^m + \cdots \tag{15c}$$

To obtain the approximated transmission conditions on the smooth boundary Γ, we extend *formally* u^e inside the membrane. We impose:

$$\begin{aligned} &\Delta u_k^e = 0, \text{in } \mathcal{O}_e,\\ &\Delta u_k^c = 0, \text{in } \mathcal{O}_c,\\ &u_k^e|_{\partial\Omega} = \delta_{0,k}\phi, \text{on } \partial\Omega. \end{aligned}$$

Using a Taylor expansion in the normal variable we infer formally:

$$u^e|_{\Gamma_\delta} = u_0^e|_\Gamma + \delta\left(u_1^c|_\Gamma + \partial_n u_0^e|_\Gamma\right) + \cdots;$$

and using the hypothesis $\Delta u_k^e = 0$ in $\mathcal{O}_e$ we infer the formal expansion:

$$\partial_n u^e|_{\Gamma_\delta} = \partial_n u_0^e|_\Gamma + \delta\left(\partial_n u_1^e|_\Gamma - \Delta|_\Gamma u_0^e|_\Gamma + 2\mathscr{H}\partial_n u_0^e|_\Gamma\right) + \cdots$$

Replacing u^e, u^m and u^c by their formal expressions (15), we write now the problems satisfied by the first two terms of the respective asymptotic development of u^e, u^m and u^c. Using the convention that the terms with negative index equal zero, we formally obtain for $k = 0, 1$:

$$\Delta u_k^e = 0, \text{in } \mathcal{O}_e, \tag{16a}$$

$$\Delta u_k^c = 0, \text{in } \mathcal{O}_c, \tag{16b}$$

$$u_k^e|_{\partial\Omega} = \delta_{0,k}\phi, \text{on } \partial\Omega. \tag{16c}$$

In the thin layer, we have:

$$\begin{aligned} &\forall (x_1, x_2, x_3) \in \Gamma \times [0, 1],\\ &\partial_{x_3}^2 u_k^m + \partial_{x_3}^2 u_{k-1}^m - 2\mathscr{H}\partial_{x_3} u_{k-1}^m = 0. \end{aligned} \tag{16d}$$

The following transmission conditions hold for u^e and u^c:

$$\left(u_k^e|_\Gamma + \partial_n u_{k-1}^e|_\Gamma\right) \circ \Psi = u_k^m(.,1), \tag{16e}$$
$$u_k^c|_\Gamma \circ \Psi = u_k^m(.,0) \tag{16f}$$

Since the normal derivatives involve the complex permittivities z_c, z_m and z_e, we have to take into account the behavior of these permittivities with respect to δ.

2.4. **Low frequency development**

In the low frequency range the complex permittivities of the domains may be written as follows:

$$z_e = \beta_e + \mathrm{i}\delta^2\alpha_e,$$
$$z_c = \beta_c + \mathrm{i}\delta^2\alpha_c,$$
$$z_m = \delta^2\left(\beta_m + \mathrm{i}\alpha_m\right).$$

Therefore, transmission conditions (14d)–(14f) imply:

$$\beta_e \partial_n u_0^e|_{\Gamma^+} = 0, \quad \beta_c \partial_n u_0^c|_{\Gamma^-} = 0, \tag{17a}$$
$$\beta_e\left(\partial_n u_1^e|_{\Gamma^+} - \Delta|_\Gamma u_0^e|_\Gamma + 2\mathscr{H}\partial_n u_0^e|_\Gamma\right) \circ \Psi = (\beta_m + \mathrm{i}\alpha_m)\partial_{x_3} u_0^m|_{x_3=1}, \tag{17b}$$
$$\beta_c \partial_n u_1^c|_{\Gamma^-} \circ \Psi = (\beta_m + \mathrm{i}\alpha_m)\partial_{x_3} u_0^m|_{x_3=0}. \tag{17c}$$

2.4.a. *Gauge condition*

Remember the definition of function F:

$$\Delta F = 0, \text{ in } \Omega \setminus \mathscr{O}_c,$$
$$\partial_n F|_\Gamma = 1, \quad F|_{\partial\Omega} = 0.$$

Since the Dirichlet boundary data ϕ of problem (14) satisfies (4), we multiply (1) by F and we integrate by parts using Green's formula to infer:

$$\int_\Gamma u^\delta|_\Gamma(\sigma)\,\mathrm{d}\sigma = \left(\frac{\delta(\beta_m + \mathrm{i}\alpha_m)}{\beta_e} - 1\right)\int_{\Gamma_\delta} \partial_n u^\delta\big|_{\Gamma_\delta^-}(\sigma)\, F|_{\Gamma_\delta}(\sigma)\,\mathrm{d}\sigma. \tag{18}$$

Since we have:

$$\int_{\Gamma_\delta} \partial_n u^\delta\big|_{\Gamma_\delta^-}(\sigma)\, F|_{\Gamma_\delta}(\sigma)\,\mathrm{d}\sigma = \int_\Gamma \frac{1}{\delta}\partial_{x_3} u^m|_{x_3=1}\, F \circ \Phi|_{x_3=1} \frac{\mathrm{d}x_1\,\mathrm{d}x_2}{1 - 2\delta\mathscr{H} + \delta^2\mathscr{K}},$$

according to the ansatz we infer the following gauge conditions :

$$\int_\Gamma \partial_{x_3} u_0^m|_{x_3=1} F|_\Gamma \circ \Psi\ \mathrm{d}x_1\,\mathrm{d}x_2 = 0, \tag{19a}$$

$$\begin{aligned}\int_\Gamma \partial_{x_3} u_1^m|_{x_3=1} F|_\Gamma \circ \Psi\ \mathrm{d}x_1\,\mathrm{d}x_2 &= \int_\Gamma u_0^c|_\Gamma(\sigma)\,\mathrm{d}\sigma - \int_\Gamma \partial_{x_3} u_0^m\ \mathrm{d}x_1\,\mathrm{d}x_2 \\ &- \int_\Gamma \left(2\mathscr{H} + (\alpha_m + \mathrm{i}\beta_m)/\beta_e\right)\partial_{x_3} u_0^m F|_\Gamma \circ \Psi\ \mathrm{d}x_1\,\mathrm{d}x_2.\end{aligned} \tag{19b}$$

2.4.b. *Identification*

We are now ready to derive the low frequency asymptotic expansion of the electric potential.

- *The* 0^{th}*order terms.* According to (17a), we obtain the following equalities:

$$\partial_n u_0^e|_{\Gamma^+} = 0,$$
$$\partial_n u_0^c|_{\Gamma^-} = 0,$$
$$\forall (x_1, x_2, x_3), \quad \partial^2_{x_3} u_0^m = 0.$$

Hence u_0^e is entirely determined by :

$$\Delta u_0^e = 0, \quad \text{in } \Omega \setminus \mathcal{O}_e, \tag{20a}$$
$$u_0^e|_{\partial\Omega} = \phi, \quad \partial_n u_0^e|_{\Gamma} = 0, \tag{20b}$$

and u_0^c equals an undefined constant since it satisfies:

$$\Delta u_0^c = 0, \quad \text{in } \mathcal{O}_c, \tag{20c}$$
$$\partial_n u_0^c|_{\Gamma} = 0. \tag{20d}$$

Therefore, using (16) for $k = 0$ we infer

$$u_0^m(x_1, x_2, x_3) = x_3\,(u_0^e|_\Gamma - u_0^c|_\Gamma)\,\mathrm{o}\,\Psi + u_0^c|_\Gamma\,\mathrm{o}\,\Psi.$$

Hence Gauge condition (19a) implies:

$$\int_\Gamma u_0^c|_\Gamma F|_\Gamma \,\mathrm{d}\sigma = \int_\Gamma u_0^e|_\Gamma F|_\Gamma \,\mathrm{d}\sigma.$$

Since u_0^c is constant and since

$$\int_\Gamma F(\sigma)\,\mathrm{d}\sigma = -\int_{\Omega\setminus\mathcal{O}_c} |\nabla F(\sigma)|^2 \,\mathrm{d}\sigma \neq 0,$$

we infer

$$u_0^c \equiv -\frac{\int_\Gamma u_0^e|_\Gamma F|_\Gamma \,\mathrm{d}\sigma}{\int_{\Omega\setminus\mathcal{O}_c} |\nabla F(\sigma)|^2 \,\mathrm{d}\sigma},$$

and $u_0^m(x_1, x_2, x_3) = x_3\,(u_0^e|_\Gamma - u_0^c|_\Gamma)\,\mathrm{o}\,\Psi + u_0^c|_\Gamma\,\mathrm{o}\,\Psi$.

- *The first order terms.* Since

$$\partial_{x_3} u_0^m = u_0^e|_\Gamma\,\mathrm{o}\,\Psi - u_0^c|_\Gamma$$

we use (17b)–(17c) to infer:

$$\Delta u_1^e = 0, \text{ in } \Omega \setminus \mathcal{O}_c, \tag{21a}$$
$$u_1^e|_{\partial\Omega} = 0, \quad \partial_n u_1^e|_{\Gamma^+} = \frac{\beta_m + \mathrm{i}\alpha_m}{\beta_e}(u_0^e|_{\Gamma^+} - u_0^c|_\Gamma) + \Delta|_\Gamma u_0^e|_{\Gamma^+}, \tag{21b}$$

and u_1^c is determined up to a constant by

$$\Delta u_1^c = 0, \text{ in } \mathcal{O}_c, \tag{21c}$$
$$\partial_n u_1^c|_{\Gamma^-} = \frac{\beta_m + \mathrm{i}\alpha_m}{\beta_c}(u_0^e|_{\Gamma^+} - u_0^c|_\Gamma). \tag{21d}$$

Moreover, the coefficient u_1^m satisfies:

$$\begin{aligned}&\partial_{x_3}^2 u_1^m = 2\mathscr{H}(u_0^e|_{\Gamma^+} \circ \Psi - u_0^c|_\Gamma),\\ &u_1^m(.,1) = u_1^e|_\Gamma \circ \Psi, \quad u_1^m(.,0) = u_1^c|_\Gamma \circ \Psi,\end{aligned}$$

hence

$$u_1^m(.,x_3) = \left(x_3(x_3-1)\mathscr{H}(u_0^e|_{\Gamma^+} \circ \Psi - u_0^c|_\Gamma) + x_3 u_1^e|_{\Gamma^+} + (1-x_3)u_1^c|_{\Gamma^-} \right) \circ \Psi.$$

To entirely determine u_1^c, and therefore u_1^m, we use (19). Actually, simple calculations lead to:

$$\int_\Gamma u_1^c(\sigma)F(\sigma)\,\mathrm{d}\sigma = \int_\Gamma \left(u_1^e(\sigma) + \left(\mathscr{H}(\sigma) + \frac{\alpha_m + \mathrm{i}\beta_m}{\beta_e} \right)(u_0^e|_{\Gamma^+} \circ \Psi - u_0^c|_\Gamma) \right) F(\sigma)\,\mathrm{d}\sigma.$$

2.4.c. *Equivalent conditions*

To obtain the equivalent conditions (5)–(6), observe that $u_0^e + \delta u_1^e$ and $u_0^c + \delta u_1^c$ satisfy:

$$\begin{aligned}&\Delta(u_0^e + \delta u_1^e) = 0, \text{ in } \Omega \setminus \mathcal{O}_c,\\ &(u_0^e + \delta u_1^e)|_{\partial\Omega} = \phi, \quad \partial_n(u_0^e + \delta u_1^e)|_{\Gamma^+} = \delta\frac{\beta_m + \mathrm{i}\alpha_m}{\beta_e} u_0^e|_{\Gamma^+} + \delta\Delta|_\Gamma u_0^e|_{\Gamma^+},\end{aligned}$$

and

$$\begin{aligned}&\Delta(u_0^c + \delta u_1^c) = 0, \text{ in } \mathcal{O}_c,\\ &\partial_n(u_0^c + \delta u_1^c)|_{\Gamma^-} = \delta\frac{\beta_m + \mathrm{i}\alpha_m}{\beta_c} u_0^e|_{\Gamma^+},\end{aligned}$$

with the Gauge condition

$$\begin{aligned}\int_\Gamma \left(u_0^c + \delta u_1^c + \delta \left(\mathscr{H}(\sigma) + \frac{(\beta_m + \mathrm{i}\alpha_m)}{\beta_e} \right) u_0^c \right) F(\sigma)\,\mathrm{d}\sigma = \int_\Gamma \Bigg(u_0^e + \delta u_1^e\\ + \delta \left(\mathscr{H}(\sigma) + \frac{(\beta_m + \mathrm{i}\alpha_m)}{\beta_e} \right) u_0^e \Bigg) F(\sigma)\,\mathrm{d}\sigma.\end{aligned}$$

To determine the terms of order 0 and 1 we have neglected the terms in δ^2. Therefore, we may replace δu_0^e and δu_0^c of the above equalities respectively by $\delta(u_0^e + \delta u_1^e)$ and $\delta(u_0^c + \delta u_1^c)$. Therefore we infer the approximated problems (5)–(6).

2.5. **Mid-frequency development**

Here, the complex permittivities of the domains may be written as follows:

$$\begin{aligned}z_e &= \beta_e + \mathrm{i}\delta\alpha_e,\\ z_c &= \beta_c + \mathrm{i}\delta\alpha_c,\\ z_m &= \delta^2\beta_m + \mathrm{i}\delta\alpha_m.\end{aligned}$$

Therefore, transmission conditions (14d)–(14f) imply:

$$\begin{cases} \beta_e \partial_n u_0^e|_{\Gamma^+} \circ \Psi = \mathrm{i}\alpha_m \partial_{x_3} u_0^m(.,1), \\ \beta_c \partial_n u_0^c|_{\Gamma^-} \circ \Psi = \mathrm{i}\alpha_m \partial_{x_3} u_0^m(.,0), \end{cases} \tag{22a}$$

$$\beta_e \left(\partial_n u_1^e|_{\Gamma^+} - \Delta|_\Gamma u_0^e|_\Gamma + 2\mathscr{H}\partial_n u_0^e|_\Gamma + \mathrm{i}\alpha_e \partial_n u_0^e|_\Gamma\right) \circ \Psi = \mathrm{i}\alpha_m \partial_{x_3} u_1^m(.,1) + \beta_m \partial_{x_3} u_0^m|_{x_3=1}, \tag{22b}$$

$$\beta_c \left(\partial_n u_1^c|_{\Gamma^-} + \mathrm{i}\alpha_c \partial_n u_0^c|_\Gamma\right) \circ \Psi = \mathrm{i}\alpha_m \partial_{x_3} u_1^m(.,0) + \beta_m \partial_{x_3} u_0^m|_{x_3=0}. \tag{22c}$$

- *The* 0^{th} *order terms.* Since $\partial_{x_3}^2 u_0^m = 0$, we infer $\partial_{x_3} u_0^m(.,1) = \partial_{x_3} u_0^m(.,0)$ hence

$$\frac{\beta_e}{\mathrm{i}\alpha_m}\partial_n u_0^e|_{\Gamma^+} = \frac{\beta_c}{\mathrm{i}\alpha_m}\partial_n u_0^c|_{\Gamma^-},$$

and

$$u_0^m(.,x_3) = -\mathrm{i}x_3 \frac{\beta_e}{\alpha_m}\partial_n u_0^e|_{\Gamma^+} + u_0^c|_{\Gamma^-}.$$

Therefore, the electric potentials u_0^e and u_0^c are solution of the following problem in Ω:

$$\begin{cases} \Delta u_0^e = 0, \text{ in } \mathcal{O}_e, \\ \Delta u_0^c = 0, \text{ in } \Omega \setminus \mathcal{O}_e, \end{cases} \tag{23a}$$

with transmission conditions

$$\beta_c\, \partial_n u_0^c|_\Gamma = \beta_e\, \partial_n u_0^e|_\Gamma, \tag{23b}$$

$$u_0^c|_\Gamma = u_0^e|_\Gamma + \frac{\mathrm{i}\beta_e}{\alpha_m}\partial_n u_0^e|_{\Gamma^+}, \tag{23c}$$

and with Dirichlet boundary condition

$$u_0^e|_{\partial\Omega} = \phi. \tag{23d}$$

- *The first order terms.* Since $\partial_{x_3}^2 u_1^m = 2\mathscr{H}\partial_{x_3} u_0^m$, we infer that the potentials u_1^e and u_1^c are solution of the following problem in Ω:

$$\begin{cases} \Delta u_1^e = 0, \text{ in } \mathcal{O}_e, \\ \Delta u_1^c = 0, \text{ in } \Omega \setminus \mathcal{O}_e, \\ u_1^e|_{\partial\Omega} = 0, \end{cases} \tag{24a}$$

with the transmission conditions

$$\beta_c \partial_n u_1^c|_\Gamma - \beta_e \partial_n u_1^e|_\Gamma = \mathrm{i}\left(\frac{\alpha_e}{\beta_c} - \alpha_c\right)\partial_n u_0^c - \beta_e \Delta|_\Gamma u_0^e|_\Gamma, \tag{24b}$$

$$u_1^c|_\Gamma - u_1^e|_\Gamma = \frac{\mathrm{i}\beta_e}{\alpha_m}\partial_n u_1^e|_{\Gamma^+} + \left(1 + \mathrm{i}\mathscr{H}\frac{\beta_e}{\alpha_m}\right)\partial_n u_0^e|_{\Gamma^+}. \tag{24c}$$

Moreover u_1^m is entirely determined by the following expression:

$$u_1^m = x_3(x_3-1)\mathscr{H}\partial_{x_3}u_0^m - x_3\frac{\mathrm{i}}{\alpha_m}\Big(\beta_c\,(\partial_n u_1^c|_{\Gamma^-} + \mathrm{i}\alpha_c\partial_n u_0^c|_{\Gamma})\,\mathrm{o}\,\Psi$$
$$- \beta_m\partial_{x_3}u_0^m|_{x_3=0}\Big) + u_1^c|_{\Gamma^-}\,\mathrm{o}\,\Psi.$$

2.5.a. *Equivalent transmission conditions*

Observe that $u_0^e + \delta u_1^e$ and $u_0^c + \delta u_1^c$ satisfy:

$$\begin{cases}\Delta(u_0^e+\delta u_1^e) = 0, \text{ in } \mathcal{O}_e,\\ \Delta(u_0^c+\delta u_1^c) = 0, \text{ in } \Omega\setminus\mathcal{O}_e,\\ (u_0^e+\delta u_1^e)|_{\partial\Omega} = \phi,\end{cases}$$

with the transmission conditions

$$\beta_c\partial_n(u_0^c+\delta u_1^c)|_\Gamma - \beta_e\partial_n(u_0^e+\delta u_1^e)|_\Gamma = \delta\mathrm{i}\left(\frac{\alpha_e}{\beta_c}-\alpha_c\right)\partial_n u_0^c|_{\Gamma^-} - \delta\beta_e\Delta|_\Gamma u_0^e|_{\Gamma^+},$$
$$(u_0^c+\delta u_1^c)|_\Gamma - (u_0^e+\delta u_1^e)|_\Gamma = \frac{\mathrm{i}\beta_e}{\alpha_m}\partial_n(u_0^e+\delta u_1^e)|_{\Gamma^+} + \delta\left(1+\mathrm{i}\mathscr{H}\frac{\beta_e}{\alpha_m}\right)\partial_n u_0^e|_{\Gamma^+}.$$

Once again, neglecting the terms in δ^2 we obtain (7).

2.6. Sketch of the proofs

A precise description of the proof is given for non-highly heterogeneous medium with thin layer in [8,10]. We just give here the sketch of the proof of Theorem 1.3, which is very similar to the proof performed in [8,10]. For a given pulsation ω, define v as follows:

$$v = \begin{cases} u_0^e+\delta u_1^e, \ \ in\ \mathcal{O}_e^\delta,\\ u_0^c+\delta u_1^c, \ \ in\ \mathcal{O}_c,\\ u_0^m+\delta u_1^m+\delta^2 p, \ \ in\ \Gamma\times(0,1),\end{cases}$$

where p is a δ-independent function, which belongs to $H^2(\Gamma\times(0,1))$ such that $w = u^\delta - v$ satisfies:

$$\Delta w = 0, \text{ in } \mathcal{O}_e^\delta\cup\mathcal{O}_c\cup\mathcal{O}_m^\delta,$$
$$w|_{\partial\Omega} = 0,$$

with the following transmission conditions

$$z_e\partial_n w|_{\Gamma_\delta^+} - z_m\partial_n w|_{\Gamma_\delta^-} = O(\delta^2),$$
$$z_m\partial_n w|_{\Gamma^+} - z_c\partial_n w|_{\Gamma^-} = O(\delta^2),$$
$$w|_{\Gamma_\delta^+} - w|_{\Gamma_\delta^-} = 0,$$
$$w|_{\Gamma^+} - w|_{\Gamma^-} = 0.$$

Then consider $\tilde w = w/|z_m(\omega)|$. Multiply by ϕ in $H^1(\Omega)$ and integrate by parts with the help of Green formula. Taking $\phi = \tilde w$ and using the well-known trace theorem on Γ we infer that

$$\|\tilde w\|_{H^1(\Omega)} = O(\delta^2/|z_m|),$$

and therefore we infer Theorem 1.3, since $w = |z_m|\tilde{w}$.

References

[1] A. Claisse, V. Ducrot, and P. Frey. Levelsets and anisotropic mesh adaptation. Submitted to AIMS, 2008.

[2] Manfredo P. do Carmo. *Differential geometry of curves and surfaces*. Prentice-Hall Inc., Englewood Cliffs, N.J., 1976. Translated from the Portuguese.

[3] B. A. Dubrovin, A. T. Fomenko, and S. P. Novikov. *Modern geometry—methods and applications. Part I*, volume 93 of *Graduate Texts in Mathematics*. Springer-Verlag, New York, second edition, 1992. The geometry of surfaces, transformation groups, and fields, Translated from the Russian by Robert G. Burns.

[4] E. C. Fear and M. A. Stuchly. Modelling assemblies of biological cells exposed to electric fields. *IEEE Trans Biomed Eng*, 45(10):1259–1271, Oct 1998.

[5] K.R. Foster and H.P. Schwan. Dielectric properties of tissues and biological materials: a critical review. *CRC in Biomedical Engineering*, 17(1):25–104, 1989.

[6] Michel Marty, Gregor Sersa, and Jean Rémi Garbay *et al.* Electrochemotherapy – an easy, highly effective and safe treatment of cutaneous and subcutaneous metastases: Results of esope (european standard operating procedures of electrochemotherapy) study. *E.J.C Supplements*, 4:3–13, 2006.

[7] S. Muñoz, J.L. Sebastián, M. Sancho, and J.M. Miranda. Transmembrane voltage induced on altered erythrocyte shapes exposed to rf fields. *Bioelectromagnetics*, 25(1):631–633 (electronic), 2004.

[8] C. Poignard. *Méthodes asymptotiques pour le calcul de champs électromagnétiques dans des milieux à couche mince. Application aux cellules biologiques*. PhD thesis, Insitut Camille Jordan. Université de Lyon, November 2006. Thesis. http://www.cmap.polytechnique.fr/∼poignard/these.html.

[9] C. Poignard. Asymptotics for steady state voltage potentials in a bidimensional highly contrasted medium with thin layer. *Math. Meth. Appl. Sci.*, July 2007. DOI: 10.1002/mma.923. http://www.cmap.polytechnique.fr/∼poignard/MMAS-31pp.html.

[10] C. Poignard. Approximate transmission conditions through a weakly oscillating thin layer. *Math. Meth. App. Sci.*, 2008. To appear. 18p. http://www.cmap.polytechnique.fr/∼poignard/membWosci-18pp.html.

[11] C. Poignard, P. Dular, R. Perrussel, L. Krähenbühl, L. Nicolas, and M. Schatzman. Approximate condition replacing thin layer. *IEEE Trans. on Mag.*, 44(6):1154–1157, 2008. http://hal.archives-ouvertes.fr/hal-00165049/fr.

[12] G. Pucihar, T. Kotnik, B. Valič, and D. Miklavčič. Numerical determination of transmembrane voltage induced on irregularly shaped cells. *Ann Biomed Eng*, 34(4):642–652, Apr 2006.

[13] G. Schwarz. *Hodge Decomposition- A method for solving boundary value problems*. Springer. Lecture notes, Berlin, 1995.

[14] J.L. Sebastián, S. Muñoz, M. Sancho, and J.M. Miranda. Analysis of the influence of the cell geometry and cell proximity effects on the electric field distribution from direct rf exposure. *Phys. Med. Biol.*, 46:213–225 (electronic), 2001.

[15] G. Serša. Application of electroporation in electrochemotherapy of tumors. In *Electroporation based Technologies and Treatment: proceedings of the international scientific workshop and postgraduate course*, pages 42–45, 14-20 November 2005. Ljubljana, SLOVENIA.

[16] J. A. Sethian. *Level set methods and fast marching methods*, volume 3 of *Cambridge Monographs on Applied and Computational Mathematics*. Cambridge University Press, Cambridge, second edition, 1999. Evolving interfaces in computational geometry, fluid mechanics, computer vision, and materials science.

[17] J. Teissié, M. Golzio, and M.P. Rols. Mechanisms of cell membrane electropermeabilization: A minireview of our present (lack of?) knownledge. *Biochimica et Biophysica Acta*, 1724:270–280, 2005.