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Modélisation mathématique pour l'imagerie membranaire

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Contents

Introduction

This thesis introduces a mathematical framework for cell membrane imaging. It aims at exhibiting the fundamental mechanisms underlying the fact that effective biological tissue electrical properties and their frequency dependence reflect the tissue composition and physiology. The objectives are twofold: (i) to understand how the dependence of the effective electrical admittivity measures the complexity of the cellular organization of the tissue; (ii) to develop electrical tissue property imaging approaches in order to improve differentiation of tissue pathologies. Mathematical and numerical models obtained in this thesis could be utilized in studying the disease status, in monitoring effectiveness of treatment in individual patients. They may also find diagnostic applications in long term goal.

Biological tissues possess characteristic distributions of electrical conductivity and permittivity [96]. Conductivity can be regarded as a measure of the ability to transport charge throughout material's volume under an applied electric field, while permittivity is a measure of the ability of the dipoles within a material to rotate (or of the material to store charge) under an applied external field. At low frequencies, biological tissues behave like a conductor, but capacitive effects become important at higher frequencies due to the membranous structures [120, 122]. The electric behavior of a biological tissue under the influence of an electric field at frequency ω can be characterized by its frequency-dependent admittivity $k_{ef} := \sigma_{ef}(\omega) + i\omega\epsilon_{ef}(\omega)$, where σ_{ef} and ϵ_{ef} are respectively its effective conductivity and permittivity.

Electrical impedance spectroscopy assesses the frequency dependence of the effective admittivity by measuring it across a range of frequencies from a few Hz to hundreds of MHz. Effective admittivity of biological tissues and its frequency dependence vary with tissue composition, membrane characteristics, intra-and extracellular fluids and other factors.

In this thesis, we prove that admittance spectroscopy provides information about the microscopic structure of the medium and physiological and pathological conditions of the tissue. Moreover, we propose an optimal control scheme for reconstructing admittivity distributions from multi-frequency micro-electrical impedance tomography and prove its local convergence and stability.

In Part I, a homogenization theory is established to quantify the effective admittivity of a tissue described as a cell suspension.

The determination of the effective, or macroscopic, property of a suspension is an enduring problem in physics [99]. It has been studied by many distinguished scientists, including Maxwell, Poisson [111], Faraday, Rayleigh [113], Fricke [61], Lorentz, Debye, and Einstein [55]. Many studies have been conducted on approximate analytic expressions for overall admittivity of a cell suspension from the knowledge of pointwise conductivity distribution, and these studies were mostly restricted to the simplified model of a strongly dilute suspension of spherical or ellipsoidal cells.

In Chapter 1 we consider a periodic suspension of identical cells of arbitrary shape. We apply at the boundary of the medium an electric field of frequency ω. The medium outside the cells has an admittivity of $k_0 := \sigma_0 + i\omega\epsilon_0$. Each cell is composed of an isotropic homogeneous core of admittivity k_0 and a thin membrane of constant thickness δ and admittivity $k_m := \sigma_m + i\omega\epsilon_m$. The thickness δ is considered to be very small relative to the typical cell size and the membrane is considered very resistive, *i.e.*, $\sigma_m \ll \sigma_0$. In this context, the potential in the medium passes an effective discontinuity over the cell boundary; the jump is proportional to its normal derivative with a coefficient of the effective thickness, given by $\delta k_0 / k_m$. The normal derivative of the potential is continuous across the cell boundaries.

We use homogenization techniques with asymptotic expansions to derive a homogenized problem and to define an effective admittivity of the medium. We prove a rigorous convergence of the initial problem to the homogenized problem via two-scale convergence.

For dilute cell suspensions, we use in Chapter 2 layer potential techniques to expand the effective admittivity in terms of cell volume fraction. Through the effective thickness, $\delta\, k_0/k_m$, the first-order term in this expansion can be expressed in terms of a membrane polarization tensor, M, that depends on the operating frequency ω. We retrieve the Maxwell-Wagner-Fricke formula for concentric circular-shaped cells. This explicit formula has been generalized in many directions: in three dimension for concentric spherical cells; to include higher power terms of the volume fraction for concentric circular and spherical cells; and to include various shapes such as concentric, confocal ellipses and ellipsoids; see [35, 36, 58, 59, 60, 95, 119, 120, 122].

The imaginary part of the membrane polarization tensor M is proven to be positive for δ small enough. Its two eigenvalues are maximal for frequencies $1/\tau_i, i = 1,2$, of order of a few MHz with physically plausible parameters values. This dispersion phenomenon well known by the biologists is referred to as the β-dispersion. The associated characteristic times τ_i correspond to Debye relaxation times. Given this, we show that different microscopic organizations of the medium can be distinguished via $\tau_i, i = 1,2$, alone. The relaxation times τ_i are computed numerically for different configurations: one circular or elliptic cell, two or three cells in close proximity. The obtained results illustrate the viability of imaging cell suspensions using the spectral properties of the membrane polarization. The Debye relaxation times are shown to be able to give the microscopic structure of the medium.

In Chapter 3, we show that our results can be extended to the random case by considering a randomly deformed periodic medium. We also derive a rigorous homogenization theory for cells (and hence interfaces) that are randomly deformed from a periodic structure by random, ergodic, and stationary deformations. We prove a new formula for the overall conductivity of a dilute suspension of randomly deformed cells. Again, the spectral properties of the membrane polarization can be used to classify different microscopic structures of the medium through their Debye relaxation times. For recent works on effective properties of dilute random media, we refer to [10, 42].

In Chapter 4 we present some numerical results to illustrate the fact that the Debye relaxation times are characteristics of microstructures of the tissue. We also show some numerical results for nondilute suspensions. We observe that in the general case, Debye relaxation times, defined in exactly the same way as for dilute suspensions in Chapter 2, are characteristics of microstructures of the tissue. Moreover, they are invariant with respect to rigid transformations. However, they do depend on the volume fraction. Therefore, in the general nondilute case, microstructure classification can only be done for fixed volume fraction. This important finding is also illustrated here.

In Part II, we propose and analyze an optimal control approach for imaging the admittivity distributions of biological tissues. We consider the imaging of admittivity distributions of biological tissues from multi-frequency micro-electrical impedance data.

Micro-electrical impedance tomography [84, 94] can be used to reconstruct a high resolution admittivity distribution from internal measurements of electrical potential at multiple frequencies. The technique uses planar arrays of micro-electrodes to nondestructively sense thin layers of biological samples [39, 84, 86, 114, 130]. It has potential applications in cell electrofusion and electroporation, cell culturing, cell differentiation and drug screening; see [33, 84, 87, 88, 93, 98, 112, 115, 133]. It is capable of high-resolution imaging. Other methods of electrical tissue property imaging using internal data are investigated in [11, 13, 14, 15, 27, 63, 123, 124, 132]. Resolution and stability enhancements are achieved from internal measurements [18, 22, 23].

To solve the admittivity imaging problem from multi-frequency micro-electrical data, we design an optimal control optimization algorithm. We show that the minimization functional is Fréchet differentiable and we compute its derivative. Then we construct an initial guess by solving a boundary value problem and prove the convergence of a minimizing sequence. It is worth emphasizing that internal potential measurements at a single frequency are known to be insufficient for reconstructing the admittivity distribution.

In Part III, we mathematically formulate the optical imaging of the spatial distributions of the transmembrane potential changes induced in cells by applied external electric fields. The use of optical detection methods for the measurement of fluorescence response to membrane electric fields was reported in the early 1970s. Since then, considerable advances have been reported [90]. In [68], it has been demonstrated experimentally that membrane potential changes can be imaged with the resolution of the optical microscopy. The key feature of this system is the combined use of an external electric field and fluorescence tomography. The fluorescent indicators are designed in such a way that they respond linearly to the electrical potential jump across the membrane. As shown in this thesis, the application of the electric field enhances the membrane fluorescence imaging and its sensitivity to the membrane.

The propagation of light through a highly scattering medium with low absorption is well described by the diffusion equation [106]. Diffuse optical imaging techniques measure the spatially-dependent absorption and scattering properties of a tissue. A light source illuminates the tissue, and detectors measure the intensity of the exiting light at the boundary of the tissue, after it undergoes multiple scattering and absorption. One can use these measurements to reconstruct, from the diffusion equation, a map of the optical parameters of the studied biological tissue [92, 118].

Diffuse optical imaging techniques use near infrared light, because absorption by biological tissue is minimal at these wavelengths, and one can then produce images deep in living subjects or samples, up to several centimeters.

These techniques can be used to image fluorescing targets, known as fluorophores, in tissues. When excited by light at a specific wavelength, fluorophores emit light at a different wavelength in order to decay to their ground state. Measurements of emitted light exiting at the boundary of the tissue, combined with measurements of residual excitation light from sources after it went through the tissue, provide an insight of the tissue optical properties. More precisely, these measurements allow us to reconstruct a map of the tissue optical parameters, the distribution of fluorophore concentration, and fluorophore lifetime, which is the time they spend in their excited state before emitting light [50, 107]. The fluorescent indicators, which can be chosen with excitation and emission wavelengths in the near infrared light spectrum, accumulate in specific areas. With such techniques, one can then localize proteins, cells or diseased tissues, visualize in vivo biological processes, and obtain measurements of the concentration in tissues of important physiological markers, such as oxygenated hemoglobin [128, 104, 105]. Detailed structural information as well as indications of pathology can be obtained from these images.

Part III provides a mathematical model for spatial distribution of membrane electrical potential changes by fluorescence diffuse optical tomography. The resolving power of the imaging method in the presence of measurement noise is derived. The proposed mathematical model can be used for cell membrane tracking with the resolution of the optical microscope.

The results in this thesis are from [16, 17, 26].

Part I

Spectroscopic imaging of a dilute cell suspension

In Part I, a homogenization theory is derived to describe the effective admittivity of cell suspensions. A new formula is reported for dilute cases that gives the frequency-dependent effective admittivity with respect to the membrane polarization. Different microstructures are shown to be distinguishable via spectroscopic measurements of the overall admittivity using the spectral properties of the membrane polarization. The Debye relaxation times associated with the membrane polarization tensor are shown to be able to give the microscopic structure of the medium. A natural measure of the admittivity anisotropy is introduced and its dependence on the frequency of applied current is derived. A Maxwell-Wagner-Fricke formula is given for concentric circular cells, and the results can be extended to the random cases. A randomly deformed periodic medium is also considered and a new formula is derived for the overall admittivity of a dilute suspension of randomly deformed cells.

Part I is organized as follows.

Chapter 1 is devoted to the analysis of the problem. It introduces the problem settings and state the main results of this work. We prove existence and uniqueness results and establish useful *a priori* estimates. We consider a periodic cell suspension and derive spectral properties of the overall conductivity.

Chapter 2 is devoted to spectroscopic imaging of a dilute suspension. We consider the problem of determining the effective property of a suspension of cells when the volume fraction goes to zero. We make use of the asymptotic expansion of the effective admittivity in terms of the volume fraction to image a permittivity inclusion. We also discuss selective spectroscopic imaging using a pulsed approach. Finally, we introduce a natural measure of the conductivity anisotropy and derive its dependence on the frequency of applied current.

In Chapter 3 we extend our results to the case of randomly deformed periodic media. In Chapter 4 we provide numerical examples that support our main findings in Part I.

Chapter 1

Homogenization of cell membranes

1.1 Problem settings and main results

The aim of this section is to introduce the problem settings and state the main results of this chapter.

1.1.1 Periodic domain

We consider the probe domain Ω to be a bounded open set of $\mathbb{R}^2$ of class $\mathcal{C}^2$. The domain contains a periodic array of cells whose size is controlled by ε. Let C be a $\mathcal{C}^{2,\eta}$ domain being contained in the unit square $Y = [0,1]^2$, see Figure 1.4. Here, $0 < \eta < 1$ and C represents a reference cell. We divide the domain Ω periodically in each direction in identical squares $(Y_{\varepsilon,n})_n$ of size ε, where

$$Y_{\varepsilon,n} = \varepsilon n + \varepsilon Y.$$

Here, $n \in N_\varepsilon := \left\{ n \in \mathbb{Z}^2 | Y_{\varepsilon,n} \cap \Omega \neq \emptyset \right\}$.

We consider that a cell $C_{\varepsilon,n}$ lives in each small square $Y_{\varepsilon,n}$. As shown in Figure 1.3, all cells are identical, up to a translation and scaling of size ε, to the reference cell C:

$$\forall n \in N_\varepsilon, \quad C_{\varepsilon,n} = \varepsilon n + \varepsilon C.$$

So are their boundaries $(\Gamma_{\varepsilon,n})_{n \in N_\varepsilon}$ to the boundary Γ of C:

$$\forall n \in N_\varepsilon, \quad \Gamma_{\varepsilon,n} = \varepsilon n + \varepsilon \Gamma.$$

Let us also assume that all the cells are strictly contained in Ω, that is for every $n \in N_\varepsilon$, the boundary $\Gamma_{\varepsilon,n}$ of the cell $C_{\varepsilon,n}$ does not intersect the boundary $\partial\Omega$:

$$\partial\Omega \cap \Big(\bigcup_{n \in N_\varepsilon} \Gamma_{\varepsilon,n} \Big) = \emptyset.$$

1.1.2 Electrical model of the cell

Set for any open set D of $\mathbb{R}^2$:

$$L_0^2(D) := \left\{ f \in L^2(D) \Big| \int_{\partial D} f(x) ds(x) = 0 \right\}$$

and

$$H^1(D) := \left\{ f \in L^2(D) \Big| |\nabla f| \in L^2(D) \right\}.$$

We consider in this section the reference cell C immersed in a domain D. We apply a sinusoidal electrical current $g \in L_0^2(\partial D)$ with angular frequency ω at the boundary of D.

The medium outside the cell, $D \setminus \overline{C}$, is a homogeneous isotropic medium with admittivity $k_0 := \sigma_0 + i\omega\epsilon_0$. The cell C is composed of an isotropic homogeneous core of admittivity k_0 and a thin membrane of constant thickness δ with admittivity $k_m := \sigma_m + i\omega\epsilon_m$. We make the following assumptions:

$$\sigma_0 > 0, \sigma_m > 0, \epsilon_0 > 0, \epsilon_m \geq 0.$$

If we apply a sinusoidal current $g(x)\sin(\omega t)$ on the boundary ∂D in the low frequency range below 10 MHz, the resulting time harmonic potential $\breve{u}$ is governed approximately by

$$\begin{cases} \nabla \cdot (k_0 + (k_m - k_0)\chi_{\Gamma^\delta})\nabla \breve{u}) = 0 \quad \text{in } D \\ k_0 \dfrac{\partial \breve{u}}{\partial n}\Big|_{\partial D} = g, \end{cases}$$

where $\Gamma^\delta := \{x \in C \ : \ \mathrm{dist}(x, \Gamma) < \delta\}$ and χ_{Γ^δ} is the characteristic function of the set Γ^δ.

The membrane thickness δ is considered to be very small compared to the typical size ρ of the cell *i.e.* $\delta/\rho \ll 1$. According to the transmission condition, the normal component of the current density $k_0 \dfrac{\partial u}{\partial n}$ can be regarded as continuous across the thin membrane Γ.

We set $\beta := \dfrac{\delta}{k_m}$. Since the membrane is very resistive, *i.e.* $\sigma_m/\sigma_0 \ll 1$, the potential u in D undergoes a jump across the cell membrane Γ, which can be approximated at first order by $\beta k_0 \dfrac{\partial u}{\partial n}$. A rigorous proof of this result, based on asymptotic expansions of layer potentials, can be found in [77].

More precisely, u is the solution of the following equations:

$$
\begin{cases}
\nabla \cdot k_0 \nabla u = 0 & \text{in } D \setminus \overline{C}, \\
\nabla \cdot k_0 \nabla u = 0 & \text{in } C, \\
k_0 \dfrac{\partial u}{\partial n}\Big|_{+} = k_0 \dfrac{\partial u}{\partial n}\Big|_{-} & \text{on } \Gamma, \\
u|_{+} - u|_{-} - \beta k_0 \dfrac{\partial u}{\partial n} = 0 & \text{on } \Gamma, \\
k_0 \dfrac{\partial u}{\partial n}\Big|_{\partial D} = g, \ \displaystyle\int_{\partial D} g(x)ds(x) = 0, \ \int_{D\setminus\overline{C}} u(x)dx = 0.
\end{cases} \tag{1.1}
$$

Here n is the outward unit normal vector and $u|_{\pm}(x)$ denotes $\lim_{t\to 0^+} u(x \pm tn(x))$ for x on the concerned boundary. Likewise, $\dfrac{\partial u}{\partial n}\Big|_{\pm} := \lim_{t\to 0^+} \nabla u(x \pm tn(x)) \cdot n(x)$.

For any open set B in $\mathbb{R}^2$, we denote $H^1_{\mathbb{C}}(B)$ the Sobolev space $H^1(B)/\mathbb{C}$ which can be represented as :

$$
H^1_{\mathbb{C}}(B) = \left\{ u \in H^1(B) \mid \int_B u(x)dx = 0 \right\}.
$$

The following result holds.

Theorem 1.1.1. *There exists a unique solution $u := (u^+, u^-)$ in $H^1_{\mathbb{C}}(D^+) \times H^1(D^-)$ to (1.1).*

Proof. To prove the well-posedness of (1.1) we introduce the following Hilbert space: $V := H^1_{\mathbb{C}}(D) \times H^1(D)$ equipped with the following natural norm for our problem:

$$
\forall u \in V \|u\|_V = \|\nabla u^+\|_{L^2(D^+)} + \|\nabla u^-\|_{L^2(D^-)} + \|u^+ - u^-\|_{L^2(\Gamma)}.
$$

We write the variational formulation of (1.1) as follows:

Find $u \in V$ such that for all $v := (v^+, v^-) \in V$:

$$
\left\{
\begin{aligned}
&\int_{D^+} k_0 \nabla u^+(x) \cdot \nabla \overline{v}^-(x)\, dx + \int_{D^-} k_0 \nabla u^+(x) \cdot \nabla \overline{v}^-(x)\, dx \\
&\qquad\qquad + \frac{1}{\beta k_0} \int_\Gamma (u^+ - u^-)\overline{(v^+ - v^-)}\, d\sigma(x) = \frac{1}{ko} \int_{\partial\Omega} g\overline{v}\, d\sigma(x).
\end{aligned}
\right.
$$

Since $\mathcal{R}e(k_0) = \sigma_0 > 0$ and $\mathcal{R}e(\dfrac{1}{\beta k_0}) = \dfrac{\sigma_m \sigma_0 + \varepsilon_m \varepsilon_0}{\delta |k_0|} > 0$, we can apply Lax-Milgram theory to obtain existence and uniqueness of a solution to problem (1.1). $\square$

We finish this section with a few numerical simulations to illustrate the typical profile of the potential u. We consider an elliptic domain D in which lives an elliptic cell. We choose to virtually apply at the boundary of D an electrical current $g = e^{i*30r}$. We take realistic values for our parameters, which are the same as those used in Chapter 4.

The real and imaginary parts of u outside and inside the cell are represented on the figure .

We can observe that the potential jumps across the cell membrane. We plot the outside and inside gradient vector fields (Figure).

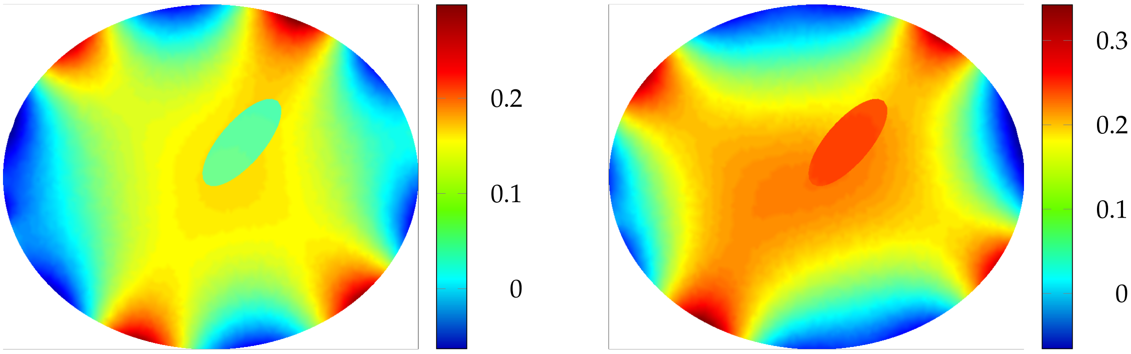

Figure 1.1: *Real and imaginary parts of the potential u outside and inside the cell.1.1.2*

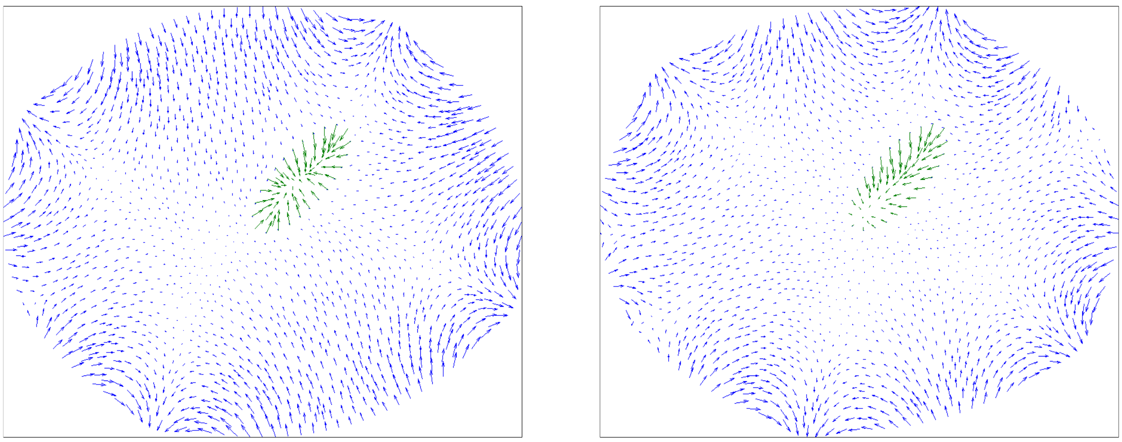

Figure 1.2: *Gradient vector fields of the real and imaginary parts of u.1.1.2*

1.1.3 Governing equation

We denote by Ω_ε^+ the medium outside the cells and Ω_ε^- the medium inside the cells:

$$\Omega_\varepsilon^+ = \Omega \cap \big(\bigcup_{n \in N_\varepsilon} Y_{\varepsilon,n} \setminus \overline{C_{\varepsilon,n}} \big), \quad \Omega_\varepsilon^- = \bigcup_{n \in N_\varepsilon} C_{\varepsilon,n}.$$

Set $\Gamma_\varepsilon := \bigcup\limits_{n \in N_\varepsilon} \Gamma_{\varepsilon,n}$. By definition, the boundaries $\partial\Omega_\varepsilon^+$ and $\partial\Omega_\varepsilon^-$ of respectively Ω_ε^+ and Ω_ε^- satisfy:

$$\partial\Omega_\varepsilon^+ = \partial\Omega \cup \Gamma_\varepsilon, \quad \partial\Omega_\varepsilon^- = \Gamma_\varepsilon.$$

We apply a sinusoidal current $g(x)\sin(\omega t)$ at $x \in \partial\Omega$, where $g \in L_0^2(\partial\Omega)$. The induced time-harmonic potential u_ε in Ω satisfies [77, 108, 109]:

$$\begin{cases} \nabla \cdot k_0 \nabla u_\varepsilon^+ = 0 & \text{in } \Omega_\varepsilon^+, \\ \nabla \cdot k_0 \nabla u_\varepsilon^- = 0 & \text{in } \Omega_\varepsilon^-, \\ k_0 \dfrac{\partial u_\varepsilon^+}{\partial n} = k_0 \dfrac{\partial u_\varepsilon^-}{\partial n} & \text{on } \Gamma_\varepsilon, \\ u_\varepsilon^+ - u_\varepsilon^- - \varepsilon \beta k_0 \dfrac{\partial u_\varepsilon^+}{\partial n} = 0 & \text{on } \Gamma_\varepsilon, \\ k_0 \dfrac{\partial u_\varepsilon^+}{\partial n}\Big|_{\partial\Omega} = g, \quad \displaystyle\int_{\partial\Omega} g(x)ds(x) = 0, \quad \int_{\Omega_\varepsilon^+} u_\varepsilon^+(x)dx = 0, & \end{cases} \tag{1.2}$$

where $u_\varepsilon = \begin{cases} u_\varepsilon^+ & \text{in } \Omega_\varepsilon^+, \\ u_\varepsilon^- & \text{in } \Omega_\varepsilon^-. \end{cases}$

Note that the previously introduced constant β, *i.e.*, the ratio between the thickness of the membrane of C and its admittivity, becomes $\varepsilon\beta$. Because the cells $(C_{\varepsilon,n})_{n \in N_\varepsilon}$ are in squares of size ε, the thickness of their membranes is given by $\varepsilon\delta$ and consequently, a factor ε appears.

1.1.4 Main results in the periodic case

We set $Y^+ := Y \setminus \overline{C}$ and $Y^- := C$.

Throughout this chapter, we assume that $\text{dist}(Y^-, \partial Y) = O(1)$. We write the solution u_ε as

$$\forall x \in \Omega \quad u_\varepsilon(x) = u_0(x) + \varepsilon u_1(x, \frac{x}{\varepsilon}) + o(\varepsilon), \tag{1.3}$$

with

$$y \longmapsto u_1(x,y) \; Y\text{-periodic and } u_1(x,y) = \begin{cases} u_1^+(x,y) \text{ in } \Omega \times Y^+, \\ u_1^-(x,y) \text{ in } \Omega \times Y^-. \end{cases}$$

The following theorem holds.

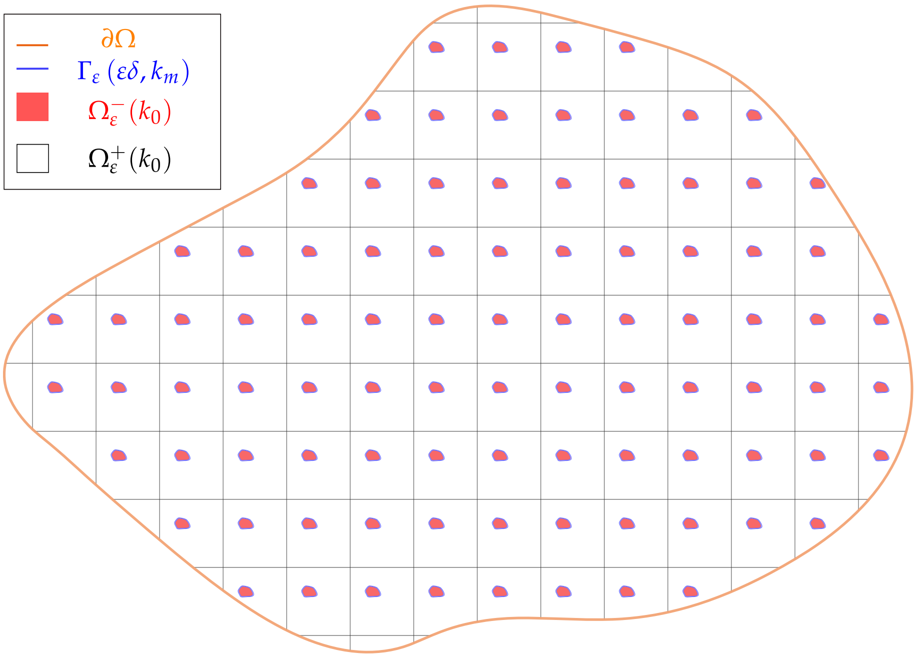

Figure 1.3: *Schematic illustration of the periodic medium* Ω.

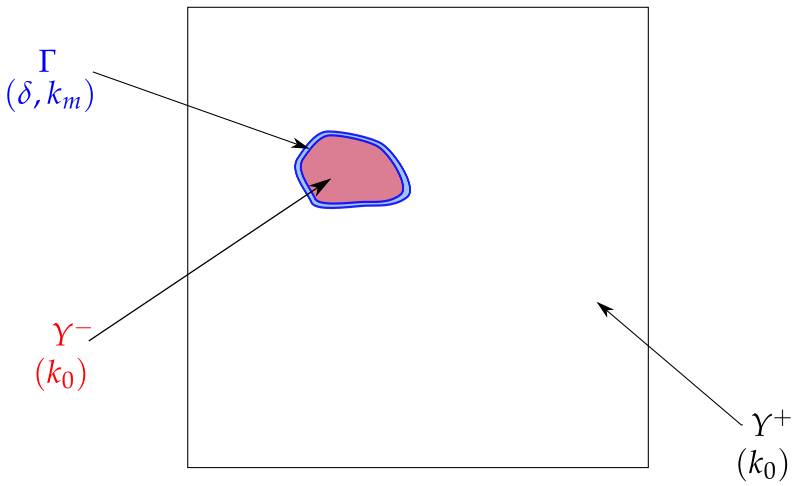

Figure 1.4: *Schematic illustration of a unit period* Y.

Theorem 1.1.2. (i) *The solution u_ε to* (1.2) *two-scale converges to u_0 and $\nabla u_\varepsilon(x)$ two-scale converges to $\nabla u_0(x) + \chi_{Y^+}(y)\nabla_y u_1^+(x,y) + \chi_{Y^-}(y)\nabla_y u_1^-(x,y)$, where $\chi_{Y^\pm}$ are the characteristic functions of $Y^\pm$.*

(ii) *The function u_0 in* (1.3) *is the solution in $H^1_{\mathbb{C}}(\Omega)$ to the following homogenized problem:*

$$\begin{cases} \nabla \cdot K^* \nabla u_0(x) = 0 & \text{in } \Omega, \\ n \cdot K^* \nabla u_0 = g & \text{on } \partial\Omega, \end{cases} \tag{1.4}$$

where K^*, the effective admittivity of the medium, is given by

$$\forall (i,j) \in \{1,2\}^2, \qquad K^*_{i,j} = k_0 \left(\delta_{ij} + \int_Y (\chi_{Y^+} \nabla w_i^+ + \chi_{Y^-} \nabla w_i^-) \cdot e_j \right), \tag{1.5}$$

and the function $(w_i)_{i=1,2}$ are the solutions of the following cell problems:

$$\begin{cases} \nabla \cdot k_0 \nabla (w_i^+(y) + y_i) = 0 & \text{in } Y^+, \\ \nabla \cdot k_0 \nabla (w_i^-(y) + y_i) = 0 & \text{in } Y^-, \\ k_0 \dfrac{\partial}{\partial n}(w_i^+(y) + y_i) = k_0 \dfrac{\partial}{\partial n}(w_i^-(y) + y_i) & \text{on } \Gamma, \\ w_i^+ - w_i^- - \beta k_0 \dfrac{\partial}{\partial n}(w_i^+(y) + y_i) = 0 & \text{on } \Gamma, \\ y \longmapsto w_i(y) \ Y\text{-periodic}. \end{cases} \tag{1.6}$$

(iii) *Moreover, u_1 can be written as*

$$\forall (x,y) \in \Omega \times Y, \;\; u_1(x,y) = \sum_{i=1}^{2} \frac{\partial u_0}{\partial x_i}(x) w_i(y). \tag{1.7}$$

We define the integral operator $\mathcal{L}_\Gamma : \mathcal{C}^{2,\eta}(\Gamma) \to \mathcal{C}^{1,\eta}(\Gamma)$, with $0 < \eta < 1$ by

$$\mathcal{L}_\Gamma[\varphi](x) = \frac{1}{2\pi} \int_\Gamma \frac{\partial^2 \ln |x-y|}{\partial n(x) \partial n(y)} \varphi(y) ds(y), \quad x \in \Gamma. \tag{1.8}$$

$\mathcal{L}_\Gamma$ is the normal derivative of the double layer potential $\mathcal{D}_\Gamma$.

Since $\mathcal{L}_\Gamma$ is positive, one can prove that the operator $I + \alpha \mathcal{L}_\Gamma : \mathcal{C}^{2,\eta}(\Gamma) \to \mathcal{C}^{1,\eta}(\Gamma)$ is a bounded operator and has a bounded inverse provided that $\Re \alpha > 0$ [49, 102].

As the fraction f of the volume occupied by the cells goes to zero, we derive an expansion of the effective admittivity for arbitrary shaped cells in terms of the volume fraction. We refer to the suspension, as periodic dilute. The following theorem holds.

Theorem 1.1.3. *The effective admittivity of a periodic dilute suspension admits the following asymptotic expansion:*

$$K^* = k_0 \left(I + fM \left(I - \frac{f}{2} M \right)^{-1} \right) + o(f^2), \tag{1.9}$$

where $\rho = \sqrt{|Y^-|}$, $f = \rho^2$,

$$M = \left(M_{ij} = \beta k_0 \int_{\rho^{-1}\Gamma} n_j \psi_i^*(y) ds(y) \right)_{(i,j)\in\{1,2\}^2}, \tag{1.10}$$

and ψ_i^* *is defined by*

$$\psi_i^* = -\left(I + \beta k_0 \mathcal{L}_{\rho^{-1}\Gamma} \right)^{-1} [n_i]. \tag{1.11}$$

1.1.5 Description of the random cells and interfaces

We describe the domains occupied by the cells. As mentioned earlier, they are formed by randomly deforming a periodic structure. We transform the aforementioned periodic structure by a random diffeomorphism $\Phi : \mathbb{R}^2 \to \mathbb{R}^2$. Let

$$\mathbb{R}_2^+ := \bigcup_{n\in\mathbb{Z}^2} (n + Y^+), \quad \mathbb{R}_2^- := \bigcup_{n\in\mathbb{Z}^2} (n + Y^-), \quad \mathbf{\Gamma} := \bigcup_{n\in\mathbb{Z}^2} (n + \Gamma).$$

The cells, the environment and the interfaces are hence deformed to $\Phi(\mathbb{R}_2^-)$, $\Phi(\mathbb{R}_2^+)$ and $\Phi(\mathbf{\Gamma})$. We emphasize that the topology of these sets are the same as before. Finally, the deformed structure is scaled to size ε, where $0 < \varepsilon \ll 1$, by the dilation operator $\varepsilon\mathbf{I}$ where $\mathbf{I}$ is the identity operator. The final sets $\varepsilon\Phi(\mathbb{R}_2^-)$, $\varepsilon\Phi(\mathbf{\Gamma})$ and $\varepsilon\Phi(\mathbb{R}_2^+)$ thus are realistic models for the random cells, membranes and the environment for the biological problem at hand.

To model the cells inside an arbitrary bounded domain Ω as in (1.2), we would like to set $\Omega_\varepsilon^+ := \Omega \cap \varepsilon\Phi(\mathbb{R}_2^-)$ and $\Gamma_\varepsilon := \Omega \cap \varepsilon\Phi(\mathbf{\Gamma})$. However, a technicality is encountered, precisely, the intersection of $\varepsilon\Phi(\mathbf{\Gamma})$ with the boundary $\partial\Omega$ may not be empty. In this case, some cells are cut by the boundary of the body, which is not physically admissible. Moreover, an arbitrary diffeomorphism Φ may allow some deformed cells in $\varepsilon\Phi(\mathbb{R}_2^-)$ to get arbitrarily close to each other. This imposes difficulties for rigorous mathematical analysis. In order to resolve these issues, we will impose a few conditions on Φ and refine the above construction in the next subsection.

1.1.6 Stationary ergodic setting

Let $(\mathcal{O}, \mathcal{F}, \mathbb{P})$ be some probability space on which $\Phi(x,\gamma) : \mathbb{R}^2 \times \mathcal{O} \to \mathbb{R}^2$ is defined. Throughout this chapter, we assume that the space $L^2(\Omega)$ is separable. For a random variable $X \in L^1(\mathcal{O}, d\mathbb{P})$, we will denote its expectation by

$$\mathbb{E}X = \int_{\mathcal{O}} X(\gamma) d\mathbb{P}(\gamma).$$

Throughout this chapter, we assume that the group $(\mathbb{Z}^2, +)$ acts on $\mathcal{O}$ by some action $\{\tau_n : \mathcal{O} \to \mathcal{O}\}_{n\in\mathbb{Z}^2}$, and that for all $n \in \mathbb{Z}^2$, τ_n is $\mathbb{P}$-preserving, that is,

$$\mathbb{P}(A) = \mathbb{P}(\tau_n A), \quad \text{for all } A \in \mathcal{F}.$$

We assume further that the action is *ergodic*, which means that for any $A \in \mathcal{F}$, if $\tau_n A = A$ for all $n \in \mathbb{Z}^2$, then necessarily $\mathbb{P}(A) \in \{0,1\}$.

Following [44], we say that a random process $F \in L^1_{\text{loc}}(\mathbb{R}^2, L^1(\mathcal{O}))$ is (discrete) *stationary* if

$$\forall n \in \mathbb{Z}^2, \quad F(x+n,\gamma) = F(x,\tau_n\gamma) \quad \text{for almost every } x \text{ and } \gamma. \tag{1.12}$$

Clearly, a deterministic periodic function is a special case of stationary process. However, we precise that the above notion of stationarity is different from the classical one, see for instance [103] and [79]. Throughout this chapter, we presume stationarity in the sense of (1.12) if not stated otherwise. What makes this notion useful is the following version of ergodic theorem [53, 73].

Proposition 1.1.1. *Let $F \in L^\infty(\mathbb{R}^2, L^1(\mathcal{O}))$ be a stationary random process. Equip $\mathbb{Z}^2$ with the norm $|n|_\infty = \max_{1\le i\le 2}|n_i|$ for all $n \in \mathbb{Z}^2$. Then*

$$\frac{1}{(2N+1)^2}\sum_{|n|_\infty \le N} F(x,\tau_n\gamma) \xrightarrow[N\to\infty]{L^\infty} \mathbb{E}F(x,\cdot) \quad \textit{for a.e. } \gamma \in \mathcal{O}.$$

This implies in particular that if the family $\{F(\frac{\cdot}{\varepsilon},\gamma)\}$ is bounded in $L^p_{\text{loc}}(\mathbb{R}^2)$, for some $p \in [1,\infty)$, then

$$F\left(\frac{x}{\varepsilon},\gamma\right) \underset{\varepsilon\to 0}{\rightharpoonup} \mathbb{E}\left(\int_Y F(x,\cdot)dx\right) \textit{ in } L^p_{\text{loc}}(\mathbb{R}^2) \textit{ for a.e. } \gamma \in \mathcal{O}.$$

The convergence holds also in the weak-$*$ sense for $p = \infty$.

We assume that for every $\gamma \in \mathcal{O}$, $\Phi(\cdot,\gamma)$ is a diffeomorphsim from $\mathbb{R}^2$ to $\mathbb{R}^2$ and that it satisfies

$$\nabla\Phi(x,\gamma) \text{ is stationary.} \tag{1.13}$$

$$\operatorname*{ess\,inf}_{\gamma\in\mathcal{O},x\in\mathbb{R}^2} \det(\nabla\Phi(x,\gamma)) = \kappa > 0, \tag{1.14}$$

$$\operatorname*{ess\,sup}_{\gamma\in\mathcal{O},x\in\mathbb{R}^2} |\nabla\Phi(x,\gamma)|_F = \kappa' > 0, \tag{1.15}$$

where $|\cdot|_F$ is the Frobenius norm and ess inf and ess sup are the essential infimum and the essentiel supremum, respectively. To avoid the intersection of $\partial\Omega$ and the random cells $\varepsilon\Phi(\mathbb{R}_2^-)$ and the collision of cells, that is when two connected components of $\varepsilon\Phi(\mathbb{R}_2^-)$ get as close as $o(\varepsilon)$, we need the further modification in the construction of cells. To this end, we assume further that

$$\|\Phi(\cdot,\gamma) - \mathbf{I}(\cdot)\|_{L^\infty(\mathbb{R}^2)} \le \frac{\operatorname{dist}(Y^-,\partial Y)}{2} \text{ for a.e. } \gamma \in \mathcal{O}. \tag{1.16}$$

Note that this implies also that $\|\Phi^{-1} - \mathbf{I}\|_{L^\infty} \le \operatorname{dist}(Y^-,\partial Y)/2$ a.s. in $\mathcal{O}$. Now, given a bounded and simply connected open set Ω with smooth boundary and a small number $\varepsilon \ll 1$, we denote by $\Omega_{1/\varepsilon}$ the scaled set $\{x \in \mathbb{R}^2 \mid \varepsilon x \in \Omega\}$. Let $\widetilde{\Omega_{1/\varepsilon}}$ be the shrunk set

$$\widetilde{\Omega_{1/\varepsilon}} := \{x \in \Omega_{1/\varepsilon} \mid \operatorname{dist}(x,\partial\Omega_{1/\varepsilon}) \ge \operatorname{dist}(Y^-,\partial Y)\}.$$

We introduce for $n \in \mathbb{Z}^2$, Y_n and $Y_n^\pm$ the translated cubes, reference cells and reference environments: $Y_n := n + Y, Y_n^\pm := n + Y^\pm$. Let $\mathcal{I}_\varepsilon \subset \mathbb{Z}^2$ be the indices of cubes Y_n such that $Y_n \Subset \widetilde{\Omega_{1/\varepsilon}}$. Note that $\mathcal{I}_\varepsilon$ corresponds to N_ε in the periodic case. We set Ω_ε^- to be

$$\Omega_\varepsilon^- := \sum_{n \in \mathcal{I}_\varepsilon} \varepsilon\Phi(Y_n^-) \tag{1.17}$$

and then $\Omega_\varepsilon^+ = \Omega \setminus \overline{\Omega_\varepsilon^-}$. We also define the following two notations:

$$E_\varepsilon := \sum_{n \in \mathcal{I}_\varepsilon} \varepsilon\Phi(Y_n) \quad \text{and} \quad K_\varepsilon := \Omega \setminus \overline{E_\varepsilon}. \tag{1.18}$$

Clearly, E_ε encloses all the cells in $\varepsilon\Phi(Y_n^-), n \in \mathcal{I}_\varepsilon$ and their immediate surroundings $\varepsilon\Phi(Y_n^+)$; K_ε is a cushion layer near the boundary that prevents the cells from touching the boundary. From the construction we see that

$$\inf_{x \in \Omega_\varepsilon^-} \operatorname{dist}(x, \partial\Omega) \geq \varepsilon \operatorname{dist}(Y^-, \partial Y) \quad \text{and} \quad \sup_{x \in K_\varepsilon} \operatorname{dist}(x, \partial\Omega) \leq (3\operatorname{dist}(Y^-, \partial Y) + \sqrt{2})\varepsilon.$$

Furthermore, we can check that

$$\sup_{n,j \in \mathcal{I}_\varepsilon, n \neq j} \quad \inf_{x \in \varepsilon\Phi(Y_n^-), y \in \varepsilon\Phi(Y_j^-)} |x - y| \geq \operatorname{dist}(Y^-, \partial Y)\varepsilon.$$

This shows that the cells in Ω are well separated, *i.e.*, with a distance comparable to (if not much larger than) the size of the cells; see Figure 1.5.

1.1.7 Main results in the random case

The first important result in the random case concerns an auxiliary problem which produces oscillating test functions that are used in the stochastic homogenization procedure. In the following theorem, a function f^{ext} in $W^{1,s}_{\text{loc}}(\mathbb{R}^2)$ is said to be an extension of $f \in W^{1,s}_{\text{loc}}(\mathbb{R}^+_2)$ if $f^{\text{ext}} = f$ on $\mathbb{R}^+_2$ and $\|f^{\text{ext}}\|_{W^{1,s}(K)} \leq C(K, \mathbb{R}^+_2)\|f\|_{W^{1,s}(\mathbb{R}^+_2 \cap K)}$, for any compact subset K.

The following theorem holds.

Theorem 1.1.4. *Let $\Phi(\cdot, \gamma)$ be a random diffeomorphism from $\mathbb{R}^2$ to $\mathbb{R}^2$ defined on the probability space $(\mathcal{O}, \mathcal{F}, \mathbb{P})$, and assume that* (1.13)(1.14)(1.15) *hold. For any fixed vector*

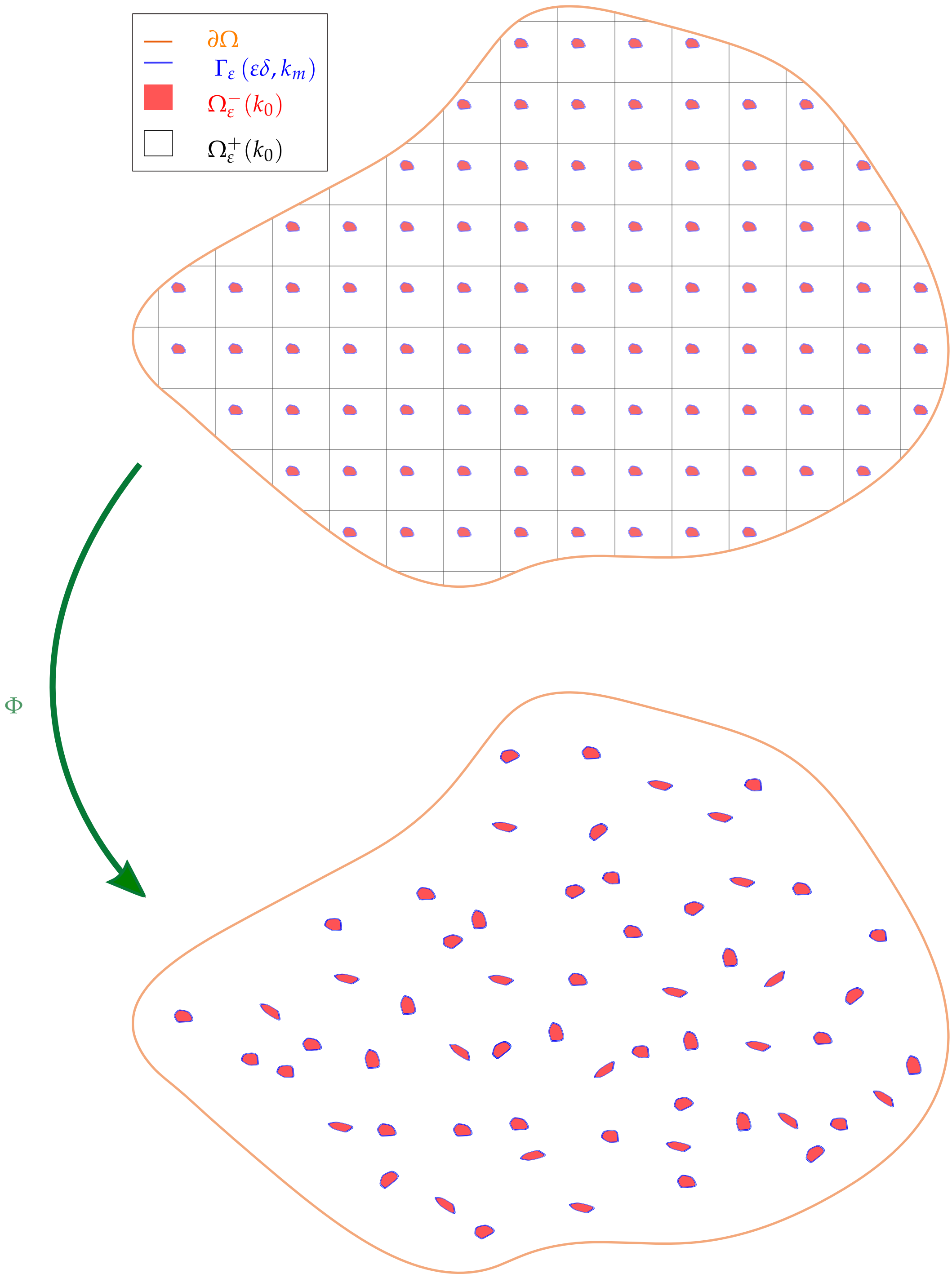

Figure 1.5: *Schematic illustration of the randomly deformed periodic medium* Ω.

$p \in \mathbb{R}^2$, the system

$$
\begin{cases}
\nabla \cdot k_0(\nabla w_p^+(y) + p) = 0 & \text{in } \Phi(\mathbb{R}_2^+, \gamma), \\
\nabla \cdot k_0(\nabla w_p^-(y) + p) = 0 & \text{in } \Phi(\mathbb{R}_2^-, \gamma), \\
k_0 \dfrac{\partial w_p^+}{\partial n}(y) - \dfrac{\partial w_p^-}{\partial n}(y) = 0 & \text{on } \Phi(\Gamma_2, \gamma), \\
w_p^+ - w_p^- - \beta k_0 \dfrac{\partial w_p^+}{\partial n}(y) = 0 & \text{on } \Phi(\Gamma_2, \gamma), \\
w_p^\pm(y,\gamma) = \widetilde{w}_p^\pm(\Phi^{-1}(y,\gamma),\gamma), & \\
\nabla \widetilde{w}_p^\pm \text{ are stationary}, & \\
\exists \tilde{w}_p^{\text{ext}} \in H^1_{\text{loc}}(\mathbb{R}^2) \text{ that extends } \tilde{w}_p^+ \quad \text{s.t. } \mathbb{E}\left(\int_Y \nabla \tilde{w}_p^{\text{ext}}(\tilde{y}, \cdot) d\tilde{y}\right) = 0, &
\end{cases}
\tag{1.19}
$$

admits a unique (up to an addition of a random variable) weak solution $w_p = w_p^+ \chi_{\Phi(\mathbb{R}_2^+)} + w_p^- \chi_{\Phi(\mathbb{R}_2^-)}$, where $w_p^\pm \in L^2(\mathcal{O}, H^1_{\text{loc}}(\Phi(\mathbb{R}_2^\pm)))$.

The precise weak formulation of the system above is postponed to Chapter 3, where the proof of this theorem is given; see (3.1). We remark that the non-unique additive random variable is not important and what matters is the fact that the gradient ∇w_p of the solution is unique. The second main result in the random case is the following homogenization theorem.

Theorem 1.1.5. *Let Ω be a bounded and connected open subset of $\mathbb{R}^2$ with regular boundary. Let Φ be a random diffeomorphism on $(\mathcal{O}, \mathcal{F}, \mathbb{P})$ satisfying* (1.13)(1.14)(1.15)(1.16). *Assume that the cells Ω_ε^- are constructed as in Section 1.1.6. Then for a.e. $\gamma \in \mathcal{O}$, the solution $u_\varepsilon(\cdot,\gamma) = (u_\varepsilon^+, u_\varepsilon^-)$ of* (1.2) *satisfies the following properties:*

(i) *We can extend $u_\varepsilon^+(\cdot,\gamma)$ to $u_\varepsilon^{\text{ext}}(\cdot,\gamma) \in H^1(\Omega)$, where $u_\varepsilon^{\text{ext}}(\cdot,\gamma)$ converges weakly, as $\varepsilon \to 0$, to a deterministic function $u_0 \in H^1(\Omega)$.*

(ii) *The function $u_\varepsilon(\cdot,\gamma)$ converges strongly in $L^2(\Omega)$ to u_0 above. Further, let Q be the trivial extension operator setting $Qf = 0$ outside the domain of f, and define*

$$
\varrho := \det\left(\mathbb{E}\int_Y \nabla\Phi(z,\cdot)dz\right)^{-1}, \quad \theta := \varrho\, \mathbb{E}\int_{Y^-} \det \nabla\Phi(z,\cdot)dz, \tag{1.20}
$$

where det *denotes the determinant. Then, Qu_ε^- converges weakly to θu_0 in $L^2(\Omega)$ with $\theta < 1$.*

(iii) *The function u_0 is the unique weak solution in $H^1_{\mathbb{C}}(\Omega)$ to the homogenized equation*

$$
\begin{cases}
\nabla \cdot K^* \nabla u_0(x) = 0, & x \in \Omega, \\
n(x) \cdot K^* \nabla u_0(x) = g, & x \in \partial\Omega,
\end{cases}
\tag{1.21}
$$

The homogenized admittivity coefficient K^* is given by $\forall (i,j) \in \{1,2\}^2$,

$$K^*_{ij} = k_0 \left(\delta_{ij} + \varrho \mathbb{E} \int_{\Phi(Y)} e_j \cdot (\chi_{\Phi(Y^+)} \nabla w^+_{e_i} + \chi_{\Phi(Y^-)} \nabla w^-_{e_i})(y, \cdot)\, dy \right), \tag{1.22}$$

where $\{e_i\}_{i=1}^2$ *is the Euclidean basis of* $\mathbb{R}^2$ *and for each* $p \in \mathbb{R}^2$, *the pair of functions* (w^+_p, w^-_p) *is the unique solution to the auxiliary system* (1.19).

In the dilute limit $\rho := \sqrt{|Y^-|} \ll 1$, we obtain the following approximation of the effective permittivity for the dilute suspension:

$$K^*_{ij} = k_0 (I + f \mathbb{E} M_{ij}) + o(f), \tag{1.23}$$

where ϱ accounts for the averaged change of volume due to the random diffeomorphism and $f := \varrho \rho^2$ is the volume fraction occupied by the cells ; the polarization matrix M is defined by

$$M_{ij} = \beta k_0 \int_{\rho^{-1}\Phi(\Gamma)} \tilde{\psi}_i n_j \, ds(\tilde{y}), \tag{1.24}$$

where

$$\tilde{\psi}_i = -(I + \beta k_0 n \cdot \nabla \mathcal{D}_{\rho^{-1}\Phi(\Gamma)})^{-1}[n_i],$$

with $\mathcal{D}_{\rho^{-1}\Phi(\Gamma)}$ the double layer potential associated to the deformed inclusion scaled to the unit length scale.

1.2 Analysis of the problem

For a fixed ε, recall that $H^1_{\mathbb{C}}(\Omega^+_\varepsilon)$ denotes the Sobolev space $H^1(\Omega^+_\varepsilon)/\mathbb{C}$, which can be represented as

$$H^1_{\mathbb{C}}(\Omega^+_\varepsilon) = \left\{ u \in H^1(\Omega^+_\varepsilon) \mid \int_{\Omega^+_\varepsilon} u(x) dx = 0 \right\}.$$

The natural functional space for (1.2) is

$$W_\varepsilon := \left\{ u = u^+ \chi^+_\varepsilon + u^- \chi^-_\varepsilon \mid u^+ \in H^1_{\mathbb{C}}(\Omega^+_\varepsilon), u^- \in H^1(\Omega^-_\varepsilon) \right\},$$

where $\chi^\pm_\varepsilon$ are the characteristic functions of the sets $\Omega^\pm_\varepsilon$. We can verify that

$$\|u\|_{W_\varepsilon} = \left(\|\nabla u^+\|^2_{L^2(\Omega^+_\varepsilon)} + \|\nabla u^-\|^2_{L^2(\Omega^-_\varepsilon)} + \varepsilon \|u^+ - u^-\|^2_{L^2(\Gamma_\varepsilon)} \right)^{\frac{1}{2}}$$

defines a norm on W_ε. In fact, as it will be seen in Proposition 1.2.2, this norm is equivalent to the standard norm on W_ε which is

$$\|u\|_{H^1_{\mathbb{C}}(\Omega^+_\varepsilon) \times H^1(\Omega^-_\varepsilon)} = \left(\|\nabla u^+\|^2_{L^2(\Omega^+_\varepsilon)} + \|\nabla u^-\|^2_{L^2(\Omega^-_\varepsilon)} + \|u^-\|^2_{L^2(\Omega^-_\varepsilon)} \right)^{\frac{1}{2}}.$$

1.2.1 Existence and uniqueness of a solution

Problem (1.2) should be understood through its weak formulation as follows: For a fixed $\varepsilon > 0$, find $u_\varepsilon \in W_\varepsilon$ such that

$$\int_{\Omega_\varepsilon^+} k_0 \nabla u_\varepsilon^+(x) \cdot \nabla \overline{v^+}(x) dx + \int_{\Omega_\varepsilon^-} k_0 \nabla u_\varepsilon^-(x) \cdot \nabla \overline{v^-}(x) ds(x)$$
$$+ \frac{1}{\varepsilon\beta} \int_{\Gamma_\varepsilon} (u_\varepsilon^+ - u_\varepsilon^-)(x) \overline{(v^+ - v^-)}(x) ds(x) = \int_{\partial\Omega} g(x) \overline{v^+}(x) ds(x), \tag{1.25}$$

for any function $v \in W_\varepsilon$.

Define the sesquilinear form $a_\varepsilon(\cdot,\cdot)$ on $W_\varepsilon \times W_\varepsilon$ by

$$a_\varepsilon(u,v) := \int_{\Omega_\varepsilon^+} k_0 \nabla u^+ \cdot \nabla \overline{v^+} dx + \int_{\Omega_\varepsilon^-} k_0 \nabla u^- \cdot \nabla \overline{v^-} dx + \frac{1}{\varepsilon\beta} \int_{\Gamma_\varepsilon} (u^+ - u^-) \overline{(v^+ - v^-)} ds. \tag{1.26}$$

Associate the following anti-linear form on W_ε to the boundary data g:

$$\ell(u) := \int_{\partial\Omega} g \overline{u^+} ds.$$

The forms a_ε and ℓ are bounded. Moreover, a_ε is coercive in the following sense

$$\Re\, k_0^{-1} a_\varepsilon(u,u) = \left(\int_{\Omega_\varepsilon^+} |\nabla u^+|^2 dx + \int_{\Omega_\varepsilon^-} |\nabla u^-|^2 dx \right) + \frac{1}{\varepsilon\beta'} \int_{\Gamma_\varepsilon} |u^+ - u^-|^2 ds \geq C \|u\|_{W_\varepsilon}^2,$$

where $\beta' := \delta(\sigma_0\sigma_m + \omega^2\epsilon_0\epsilon_m)/(\sigma_m^2 + \omega^2\epsilon_m^2)$. Consequently, due to the Lax–Milgram theorem we have existence and uniqueness for (1.2) for each fixed ε and for every $\gamma \in \mathcal{O}$. Note that C can be chosen independent of ε.

Proposition 1.2.1. *Let $g \in H^{-1/2}(\partial\Omega)$. There exists a unique $u_\varepsilon \in W_\varepsilon$ so that*

$$a_\varepsilon(u_\varepsilon, \varphi) = \ell(\varphi), \quad \forall \varphi \in W_\varepsilon. \tag{1.27}$$

To end this subsection we remark that the two norms on W_ε are equivalent.

Proposition 1.2.2. *The norm $\|\cdot\|_{W_\varepsilon}$ is equivalent with the standard norm on $H^1_{\mathbb{C}}(\Omega_\varepsilon^+) \times H^1(\Omega_\varepsilon^-)$. Moreover, we can find two positive constants $C_1 < C_2$, independent of ε, so that*

$$C_1 \|u\|_{W_\varepsilon} \leq \|u\|_{H^1_{\mathbb{C}} \times H^1} \leq C_2 \|u\|_{W_\varepsilon}, \tag{1.28}$$

for any $u \in H^1_{\mathbb{C}}(\Omega_\varepsilon^+) \times H^1(\Omega_\varepsilon^-)$.

Similar equivalence relation was established by Monsurrò [100], whose method can be adapted easily to the current case. For the sake of completeness, we present the details in Appendix A.3.

1.2.2 Energy estimate

For any fixed $\gamma \in \mathcal{O}$ and a sequence of $\varepsilon \to 0$, by solving (1.2) we obtain the sequence $u_\varepsilon = u_\varepsilon^+ \chi_\varepsilon^+ + u_\varepsilon^- \chi_\varepsilon^-$. We obtain some *a priori* estimates for u_ε.

We first recall that the extension theorem A.1.2 yields a Poincaré–Wirtinger inequality in $H^1_{\mathbb{C}}(\Omega_\varepsilon^+)$ with a constant independent of ε. Indeed, Corollary A.2.1 shows that for all $v^+ \in H^1_{\mathbb{C}}(\Omega_\varepsilon^+)$, there exists a constant C, independent of ε, such that

$$\|v^+\|_{L^2(\Omega_\varepsilon^+)} \leq C\|\nabla v^+\|_{L^2(\Omega_\varepsilon^+)}.$$

Similarly, we can find a constant, independent of ε, by applying the trace theorem in $H^1(\Omega_\varepsilon^+)$. Using Corollary A.2.2, the following result holds.

Proposition 1.2.3. *Let $g \in H^{-\frac{1}{2}}(\partial\Omega)$. For any $\gamma \in \mathcal{O}$, let $\Omega = \Omega_\varepsilon^+ \cup \Gamma_\varepsilon \cup \Omega_\varepsilon^-$. Then there exist constants C's, independent of ε and γ, such that the solution u_ε to* (1.2) *satisfies the following estimates:*

$$\|\nabla u_\varepsilon^+\|_{L^2(\Omega_\varepsilon^+)} + \|\nabla u_\varepsilon^-\|_{L^2(\Omega_\varepsilon^-)} \leq C|k_0|^{-1}\|g\|_{H^{-\frac{1}{2}}(\partial\Omega)}, \tag{1.29}$$

$$\|u_\varepsilon^+ - u_\varepsilon^-\|_{L^2(\Gamma_\varepsilon)} \leq C|k_0|^{-1}\sqrt{\varepsilon\beta'}\|g\|_{H^{-\frac{1}{2}}(\partial\Omega)}. \tag{1.30}$$

Proof. By taking $\varphi = u_\varepsilon$ in (1.27), and taking the real part of resultant equality, we get

$$\|\nabla u_\varepsilon^+\|^2_{L^2(\Omega_\varepsilon^+)} + \|\nabla u_\varepsilon^-\|^2_{L^2(\Omega_\varepsilon^-)} + (\varepsilon\beta')^{-1}\|u_\varepsilon^+ - u_\varepsilon^-\|^2_{L^2(\Gamma_\varepsilon)} = \Re k_0^{-1}\langle g, u_\varepsilon^+\rangle. \tag{1.31}$$

Here $\langle g, u_\varepsilon^+\rangle = \int_{\partial\Omega} g\overline{u_\varepsilon^+}\,ds$ is the pairing on $H^{-\frac{1}{2}}(\partial\Omega) \times H^{\frac{1}{2}}(\partial\Omega)$, for which we have the estimate

$$|\langle g, u_\varepsilon^+\rangle| \leq \|g\|_{H^{-\frac{1}{2}}(\partial\Omega)}\|u_\varepsilon^+\|_{H^{\frac{1}{2}}(\partial\Omega)} \leq C_1\|g\|_{H^{-\frac{1}{2}}(\partial\Omega)}\|u_\varepsilon^+\|_{H^1(\Omega_\varepsilon^+)}.$$

thanks to the Cauchy - Schwartz inequality and Corollary (A.2.2). C_1 is here a constant which does not depend on ε.

Applying Proposition (1.2.2) yields

$$|\langle g, u_\varepsilon^+\rangle| \leq C_2\|g\|_{H^{-\frac{1}{2}}(\partial\Omega)}\|u_\varepsilon\|_{W_\varepsilon},$$

with a constant C_2 independent of ε.

Using this in (1.31) along with the coercivity of a we get

$$\|u_\varepsilon\|_{W_\varepsilon} \leq C_3|k_0|^{-1}\|g\|_{H^{-\frac{1}{2}}(\partial\Omega)},$$

where C_3 is still independent of ε.

It follows also that

$$|\langle g, u_\varepsilon^+\rangle| \leq C_2C_3|k_0|^{-1}\|g\|_{H^{-\frac{1}{2}}(\partial\Omega)}.$$

Substitute this estimate into the right-hand side of (1.31), we get the desired estimates. □

Next, we apply the extension theorem (Theorem A.1.2) to obtain a bounded sequence in $H^1(\Omega)$ for which we can extract a converging subsequence.

Proposition 1.2.4. *Suppose that the same conditions of the previous proposition hold. Let* $P_\gamma^\varepsilon : H^1(\Omega_\varepsilon^+) \to H^1(\Omega)$ *be the extension operator of Theorem A.1.2. Then we have*

$$\|P_\gamma^\varepsilon u_\varepsilon^+\|_{H^1(\Omega)} \leq C|k_0|^{-1}\|g\|_{H^{-\frac{1}{2}}(\partial\Omega)}, \tag{1.32}$$

and

$$\|P_\gamma^\varepsilon u_\varepsilon^+ - u_\varepsilon\|_{L^2(\Omega)} \leq C\varepsilon|k_0|^{-1}(1+\sqrt{\beta'})\|g\|_{H^{-\frac{1}{2}}(\partial\Omega)}.$$

Proof. The first inequality is a direct result of (A.11), (A.11), (A.13) and (1.29). For the second inequality, we have

$$\begin{aligned}\|P_\gamma^\varepsilon u_\varepsilon^+ - u_\varepsilon\|_{L^2(\Omega)} &= \|P_\gamma^\varepsilon u_\varepsilon^+ - u_\varepsilon^-\|_{L^2(\Omega_\varepsilon^-)} \\ &\leq C\sqrt{\varepsilon}\|P_\gamma^\varepsilon u_\varepsilon^+ - u_\varepsilon^-\|_{L^2(\Gamma_\varepsilon)} + C\varepsilon\|\nabla(P_\gamma^\varepsilon u_\varepsilon^+ - u_\varepsilon^-)\|_{L^2(\Omega_\varepsilon^-)}.\end{aligned}$$

Here, we have used estimate (A.18). Now, $\|P_\gamma^\varepsilon u_\varepsilon^+ - u_\varepsilon^-\|_{L^2(\Gamma_\varepsilon)} = \|u_\varepsilon^+ - u_\varepsilon^-\|_{L^2(\Gamma_\varepsilon)}$ is bounded in (1.30). The second term is bounded from above by

$$C\varepsilon\|\nabla P_\gamma^\varepsilon u_\varepsilon^+\|_{L^2(\Omega_\varepsilon^-)} + C\varepsilon\|\nabla u_\varepsilon^-\|_{L^2(\Omega_\varepsilon^-)} \leq C\varepsilon(\|\nabla u_\varepsilon^+\|_{L^2(\Omega_\varepsilon^+)} + \|\nabla u_\varepsilon^-\|_{L^2(\Omega_\varepsilon^-)}),$$

where we have used again (A.11). This gives the desired estimates. □

Remark 1.2.1. *As a consequence of the previous proposition, we get a sequence in* $H^1(\Omega)$*, namely* $P_\gamma^\varepsilon u_\varepsilon^+$*, which is a good estimate of* u_ε *in* $L^2(\Omega)$ *and from which we can extract a subsequence weakly converging in* $H^1(\Omega)$ *and strongly in* $L^2(\Omega)$*.*

1.3 Homogenization

We follow [8, 9] to derive a homogenized problem for the model with two-scale asymptotic expansions and to prove a rigorous two-scale convergence. In [100], the homogenization of an analogue problem is developed and proved with another method.

1.3.1 Two-scale asymptotic expansions

We assume that the solution u_ε admits the following two-scale asymptotic expansion

$$\forall x \in \Omega \;\; u_\varepsilon(x) = u_0(x) + \varepsilon u_1(x, \frac{x}{\varepsilon}) + o(\varepsilon),$$

with

$$y \longmapsto u_1(x,y)\; Y\text{-periodic and } u_1(x,y) = \begin{cases} u_1^+(x,y) \text{ in } \Omega \times Y^+, \\ u_1^-(x,y) \text{ in } \Omega \times Y^-. \end{cases}$$

We choose a test function φ_ε of the same form as u_ε:

$$\forall x \in \Omega, \;\; \varphi_\varepsilon(x) = \varphi_0(x) + \varepsilon\varphi_1(x, \frac{x}{\varepsilon}),$$

with φ_0 smooth in Ω, $\varphi_1(x,.)$ Y-periodic,

$$\varphi_1(x,y) = \begin{cases} \varphi_1^+(x,y) \text{ in } \Omega \times Y^+, \\ \varphi_1^-(x,y) \text{ in } \Omega \times Y^-, \end{cases}$$

and $\varphi_1^\pm$ smooth in $\Omega \times Y^\pm$.

In order to prove items (ii) and (iii) in Theorem 1.1.2, we perform an asymptotic expansion of the variational formulation (1.27). We thus inject these ansatz in the variational formulation and only consider the order 0 of the different integrals.

At order 0,

$$\nabla u_\varepsilon(x) = \nabla u_0(x) + \nabla_y u_1(x, \frac{x}{\varepsilon}) + o(\varepsilon).$$

Thanks to Lemma 1.3.1, we then have for the two first integrals:

$$\int_{\Omega_\varepsilon^+} k_0 \left(\nabla u_0(x) + \nabla_y u_1^+(x, \frac{x}{\varepsilon})\right) \cdot \left(\nabla \overline{\varphi}_0(x) + \nabla_y \overline{\varphi}_1^+(x, \frac{x}{\varepsilon})\right) dx$$
$$= \int_\Omega \int_{Y^+} k_0 \left(\nabla u_0(x) + \nabla_y u_1^+(x,y)\right) \cdot \left(\nabla \overline{\varphi}_0(x) + \nabla_y \overline{\varphi}_1^+(x,y)\right) dxdy + o(\varepsilon)$$

and

$$\int_{\Omega_\varepsilon^-} k_0 \left(\nabla u_0(x) + \nabla_y u_1^-(x, \frac{x}{\varepsilon})\right) \cdot \left(\nabla \overline{\varphi}_0(x) + \nabla_y \overline{\varphi}_1^-(x, \frac{x}{\varepsilon})\right) dx$$
$$= \int_\Omega \int_{Y^-} k_0 \left(\nabla u_0(x) + \nabla_y u_1^-(x,y)\right) \cdot \left(\nabla \overline{\varphi}_0(x) + \nabla_y \overline{\varphi}_1^-(x,y)\right) dxdy + o(\varepsilon).$$

We write the third integral in (1.26) as the sum, over all squares $Y_{\varepsilon,n}$, of integrals on the boundaries $\Gamma_{\varepsilon,n}$. We have

$$\frac{1}{\beta\varepsilon} \int_{\Gamma_\varepsilon} \left(u_\varepsilon^+(x, \frac{x}{\varepsilon}) - u_\varepsilon^-(x, \frac{x}{\varepsilon})\right) \left(\overline{\varphi}_\varepsilon^+(x, \frac{x}{\varepsilon}) - \overline{\varphi}_\varepsilon^-(x, \frac{x}{\varepsilon})\right) ds(x)$$
$$= \frac{1}{\beta\varepsilon} \sum_{n \in N_\varepsilon} \int_{\Gamma_{\varepsilon,n}} \left(u_\varepsilon^+(x, \frac{x}{\varepsilon}) - u_\varepsilon^-(x, \frac{x}{\varepsilon})\right) \left(\overline{\varphi}_\varepsilon^+(x, \frac{x}{\varepsilon}) - \overline{\varphi}_\varepsilon^-(x, \frac{x}{\varepsilon})\right) ds(x).$$

Let $x_{0,n}$ be the center of $Y_{\varepsilon,n}$ for each $n \in N_\varepsilon$. We perform Taylor expansions with respect to the variable x around $x_{0,n}$ for all functions $(u_i)_{i\in\{1,2\}}$ and $(\varphi_i)_{i\in\{1,2\}}$ on $Y_{\varepsilon,n}$. After the change of variables $\varepsilon(y - y_{0,n}) = x - x_{0,n}$, we obtain that

$$u_\varepsilon(x) = u_0(x_{0,n}) + \varepsilon u_1(x,y) + \varepsilon(y - y_{0,n}) \cdot \nabla u_0(x_{0,n}) + o(\varepsilon),$$
$$\varphi_\varepsilon(x) = \varphi_0(x_{0,n}) + \varepsilon \varphi_1(x,y) + \varepsilon(y - y_{0,n}) \cdot \nabla \varphi_0(x_{0,n}) + o(\varepsilon).$$

Consequently, the third integral in the variational formulation (1.27) becomes

$$\frac{\varepsilon^2}{\beta} \sum_{n \in N_\varepsilon} \int_{\Gamma_n} \left(u_1^+(x_{0,n}, y) - u_1^-(x_{0,n}, y)\right) \left(\overline{\varphi}_1^+(x_{0,n}, y) - \overline{\varphi}_1^-(x_{0,n}, y)\right) ds(y).$$

Finally, Lemma 1.3.1 gives us that

$$\frac{1}{\varepsilon\beta}\int_{\Gamma_\varepsilon}\left(u_\varepsilon^+ - u_\varepsilon^-\right)\left(\overline{\varphi}_\varepsilon^+ - \overline{\varphi}_\varepsilon^-\right) ds$$

$$= \frac{1}{\beta}\int_\Omega\int_\Gamma \left(u_1^+(x,y) - u_1^-(x,y)\right)\left(\overline{\varphi}_1^+(x,y) - \overline{\varphi}_1^-(x,y)\right) dxds(y) + o(\varepsilon).$$

Moreover, we can easily see that

$$\int_{\partial\Omega} g\overline{\varphi}_\varepsilon^+ ds = \int_{\partial\Omega} g\overline{\varphi}_0 ds + o(\varepsilon).$$

The order 0 of the variational formula is thus given by

$$\begin{aligned}
& \int_\Omega\int_{Y^+} k_0\left(\nabla u_0(x) + \nabla_y u_1^+(x,y)\right)\cdot\left(\nabla\overline{\varphi}_0(x) + \nabla_y\overline{\varphi}_1^+(x,y)\right) dxdy \\
+ & \int_\Omega\int_{Y^-} k_0\left(\nabla u_0(x) + \nabla_y u_1^-(x,y)\right)\cdot\left(\nabla\overline{\varphi}_0(x) + \nabla_y\overline{\varphi}_1^-(x,y)\right) dxdy \\
+ & \frac{1}{\beta}\int_\Omega\int_\Gamma \left(u_1^+(x,y) - u_1^-(x,y)\right)\left(\overline{\varphi}_1^+(x,y) - \overline{\varphi}_1^-(x,y)\right) dxds(y) \\
- & \int_{\partial\Omega} g(x)\overline{\varphi}_0(x) ds(x) = 0.
\end{aligned}$$

By taking $\varphi_0 = 0$, it follows that

$$\begin{aligned}
& \int_\Omega\int_{Y^+} k_0\left(\nabla u_0(x) + \nabla_y u_1^+(x,y)\right)\cdot\nabla_y\overline{\varphi}_1^+(x,y) dxdy \\
+ & \int_\Omega\int_{Y^-} k_0\left(\nabla u_0(x) + \nabla_y u_1^-(x,y)\right)\cdot\nabla_y\overline{\varphi}_1^-(x,y) dxdy \\
+ & \frac{1}{\beta}\int_\Omega\int_\Gamma \left(u_1^+(x,y) - u_1^-(x,y)\right)\left(\overline{\varphi}_1^+(x,y) - \overline{\varphi}_1^-(x,y)\right) dxds(y) = 0,
\end{aligned}$$

which is exactly the variational formulation of the cell problem (1.6) and definition (1.7) of u_1.

By taking $\varphi_1 = 0$, we recover the variational formulation of the homogenized problem (1.4):

$$\begin{aligned}
& \int_\Omega\int_{Y^+} k_0\left(\nabla u_0(x) + \nabla_y u_1^+(x,y)\right)\cdot\nabla\overline{\varphi}_0(x) dxdy \\
+ & \int_\Omega\int_{Y^-} k_0\left(\nabla u_0(x) + \nabla_y u_1^-(x,y)\right)\cdot\nabla\overline{\varphi}_0(x) dxdy \\
- & \int_{\partial\Omega} g(x)\overline{\varphi}_0(x) ds(x) = 0.
\end{aligned}$$

We introduce some function spaces, which will be very useful in the following:

- $C_\sharp^\infty(D)$ is the space of functions, which are Y - periodic and in $C^\infty(D)$,

- $L^2_\sharp(D)$ is the completion of $C^\infty_\sharp(D)$ in the L^2-norm,
- $H^1_\sharp(D)$ is the completion of $C^\infty_\sharp(D)$ in the H^1-norm,
- $L^2(\Omega, H^1_\sharp(D))$ is the space of square integrable functions on Ω with values in the space $H^1_\sharp(D)$,
- $\mathcal{D}(\Omega)$ is the space of infinitely smooth functions with compact support in Ω,
- $\mathcal{D}(\Omega, C^\infty_\sharp(D))$ is the space of infinitely smooth functions with compact support in Ω and with values in the space $C^\infty_\sharp$,

where D is Y, Y^+, Y^- or Γ.

The following lemma was used in the preceding proof. It follows from [8, Lemma 3.1].

Lemma 1.3.1. *Let f be a smooth function. We have*

$$(i) \quad \varepsilon^2 \sum_{n\in N_\varepsilon} \int_{\Gamma_{\varepsilon,n}} f(x_{0,n}, y) ds(y) = \int_\Omega \int_\Gamma f(x,y) dx ds(y) + o(\varepsilon);$$

$$(ii) \quad \int_{\Omega_\varepsilon^+} f(x, \frac{x}{\varepsilon})\, dx = \int_\Omega \int_{Y^+} f(x,y)\, dxdy + o(\varepsilon)$$

$$\text{and} \quad \int_{\Omega_\varepsilon^-} f(x, \frac{x}{\varepsilon})\, dx = \int_\Omega \int_{Y^-} f(x,y)\, dxdy + o(\varepsilon).$$

We prove that the following lemmas hold.

Lemma 1.3.2. *The homogenized problem admits a unique solution in $H^1_{\mathbb{C}}(\Omega)$.*

Proof. The effective admittivity can be rewritten as

$$\begin{aligned} K^*_{i,j} &= k_0 \int_{Y^+} (\nabla w_i^+ + e_i) \cdot (\nabla \overline{w_j^+} + e_j) dx + k_0 \int_{Y^-} (\nabla w_i^- + e_i) \cdot (\nabla \overline{w_j^-} + e_j) dx \\ &+ \frac{1}{\beta} \int_\Gamma (w_i^+ - w_i^-)(\overline{w_j^+} - \overline{w_j^-}) ds, \quad i,j = 1,2. \end{aligned}$$

Therefore, it follows that, for $\xi = (\xi_1, \xi_2) \in \mathbb{R}^2$,

$$K^* \xi \cdot \xi = k_0 \int_{Y^+} |\nabla w^+ + \xi|^2 dx + k_0 \int_{Y^-} |\nabla w^- + \xi|^2 dx + \frac{1}{\beta} \int_\Gamma |w^+ - w^-|^2 ds,$$

where $w = \sum_i \xi_i w_i$. Since $\Re e \beta \geq 0$,

$$K^* \xi \cdot \xi \geq k_0 \int_{Y^+} |\nabla w^+ + \xi|^2 dx + k_0 \int_{Y^-} |\nabla w^- + \xi|^2 dx.$$

Consequently, it follows from [6] that there exist two positive constants C_1 and C_2 such that

$$C_1 |\xi|^2 \leq \Re e K^* \xi \cdot \xi \leq C_2 |\xi|^2.$$

Standard elliptic theory yields existence and uniqueness of a solution to the homogenized problem in $H^1_{\mathbb{C}}(\Omega)$. $\square$

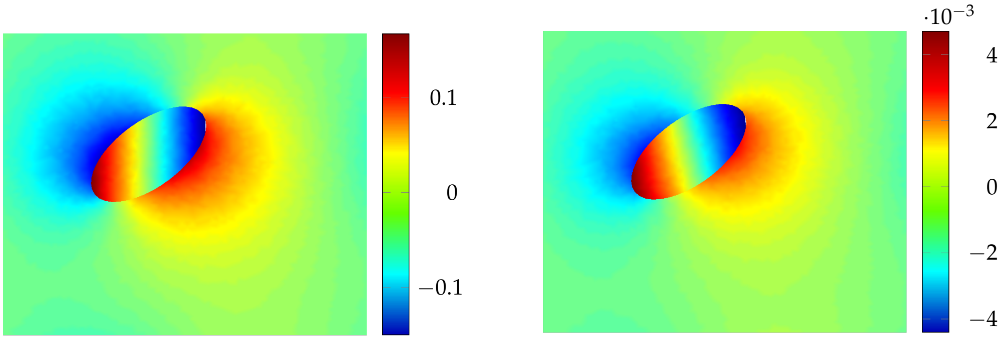

Figure 1.6: *Real and imaginary parts of the cell problem solution w_1.*

Lemma 1.3.3. *The cell problem (1.6) admits a unique solution in $H^1_\sharp(Y^+)/\mathbb{C} \times H^1_\sharp(Y^-)$.*

Proof. Let us introduce the Hilbert space

$$W := \left\{ v := v^+ \chi_{Y^+} + v^- \chi_{Y^-} | (v^+, v^-) \in H^1_{\mathbb{C}}(Y^+) \times H^1(Y^-) \right\},$$

equipped with the norm

$$\|v\|_W^2 = \|\nabla v^+\|^2_{L^2(Y^+)} + \|\nabla v^-\|^2_{L^2(Y^-)} + \|v^+ - v^-\|^2_{L^2(\Gamma)}.$$

We consider the following problem:

$$\begin{cases} \text{Find } w_i \in W_\sharp \text{ such that for all } \varphi \in W_\sharp \\ \displaystyle\int_{Y^+} k_0 \nabla w_i^+(y) \cdot \nabla \overline{\varphi}^+(y) dy + \int_{Y^-} k_0 \nabla w_i^-(y) \cdot \nabla \overline{\varphi}^-(y) dy \\ \displaystyle\qquad + \frac{1}{\beta} \int_\Gamma \left(w_i^+ - w_i^-\right)(y) \left(\overline{\varphi}^+ - \overline{\varphi}^-\right)(y) ds(y) = \\ \displaystyle\qquad\qquad - \int_{Y^+} k_0 \nabla y_i \cdot \nabla \overline{\varphi}^+(y) dy - \int_{Y^-} k_0 \nabla y_i \cdot \nabla \overline{\varphi}^-(y) dy. \end{cases} \tag{1.33}$$

Lax–Milgram theorem gives us existence and uniqueness of a solution. Moreover, one can show that this ensures the existence of a unique solution in $H^1_\sharp(Y^+)/\mathbb{C} \times H^1_\sharp(Y^-)$ for the cell problem (1.6). □

We present in the following numerical examples the real and imaginary parts of the solutions w_1 and w_2 of the cell problems.

1.3.2 Convergence

We present in this section a rigorous proof of the convergence of the initial problem to the homogenized one. We use for this purpose the two-scale convergence technique and hence need first of all some bounds on u_ε to ensure the convergence.

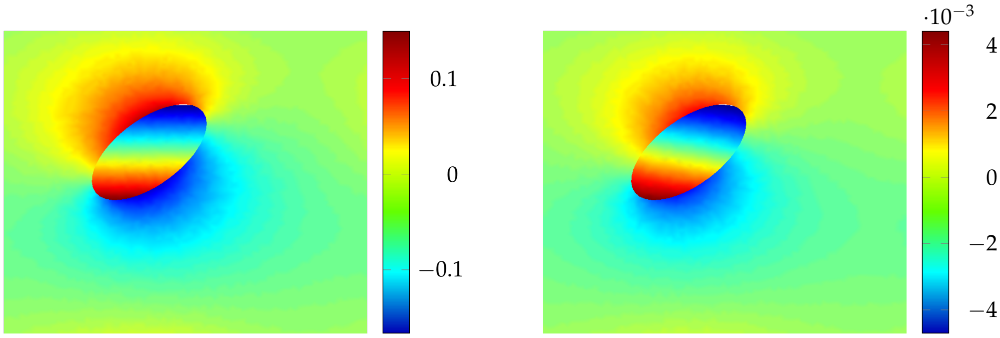

Figure 1.7: *Real and imaginary parts of the cell problem solution* w_2.

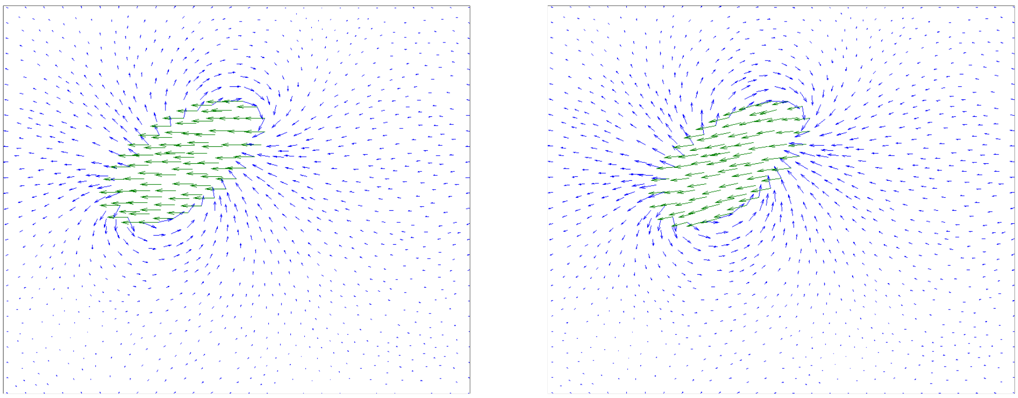

Figure 1.8: *Gradient vector field of the real and imaginary parts of* w_1.

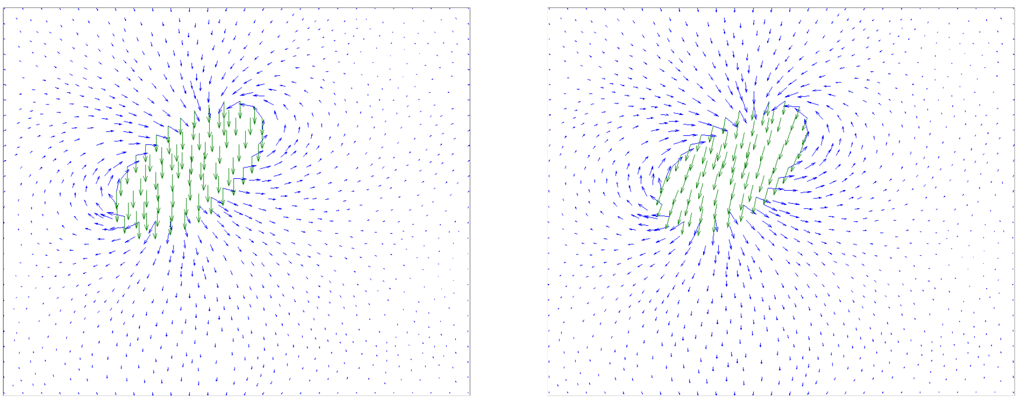

Figure 1.9: *Gradient vector field of the real and imaginary parts of* w_2.

A priori estimates

Theorem 1.3.1. *The function u_ε^+ is uniformly bounded with respect to ε in $H^1(\Omega_\varepsilon^+)$, i.e., there exists a constant C, independent of ε, such that*

$$\|u_\varepsilon^+\|_{H^1(\Omega_\varepsilon^+)} \leq C.$$

Proof. Combining (1.29) and Poincaré - Wirtinger inequality, we obtain immediately the wanted result. □

The proof of the following result follows the one of Lemma 2.8 in [100].

Lemma 1.3.4. *There exists a constant C, which does not depend on ε, such that for all $v \in W_\varepsilon$:*

$$\|v^-\|_{L^2(\Omega_\varepsilon^-)} \leq C\|v\|_{W_\varepsilon}.$$

Proof. We write the norm $\|v^-\|_{L^2(\Omega_\varepsilon^-)}$ as a sum over all the cells.

$$\|v^-\|^2_{L^2(\Omega_\varepsilon^-)} = \sum_{n\in N_\varepsilon} \|v^-\|^2_{L^2(Y_{\varepsilon,n}^-)} = \sum_{n\in N_\varepsilon} \int_{Y_{\varepsilon,n}^-} |v^-(x)|^2 dx.$$

We perform the change of variable $y = \dfrac{x}{\varepsilon}$ and get

$$\|v^-\|^2_{L^2(\Omega_\varepsilon^-)} = \varepsilon^2 \sum_{n\in N_\varepsilon} \int_{Y_n^-} |v_\varepsilon^-(y)|^2 dy, \tag{1.34}$$

where $v_\varepsilon^-(y) := v^-(\varepsilon y)$ for all $y \in Y^-$ and $Y_n^- = n + Y^-$ with $n \in N_\varepsilon$.

Recall that W denotes the following Hilbert space:

$$W := \left\{ v := v^+\chi_{Y^+} + v^-\chi_{Y^-} | (v^+, v^-) \in H^1_{\mathbb{C}}(Y^+) \times H^1(Y^-) \right\},$$

equipped with the norm:

$$\|v\|^2_W = \|\nabla v^+\|^2_{L^2(Y^+)} + \|\nabla v^-\|^2_{L^2(Y^-)} + \|v^+ - v^-\|^2_{L^2(\Gamma)}.$$

We first prove that there exists a constant C_1, independent of ε, such that for every $v \in W$:

$$\|v^-\|_{L^2(Y^-)} \leq C_1\|v\|_W. \tag{1.35}$$

We proceed by contradiction. Suppose that for any $n \in \mathbb{N}^*$, there exists $v_n \in W_\varepsilon$ such that

$$\|v_n^-\|_{L^2(Y^-)} = 1 \quad \text{and} \quad \|v_n\|_W \leq \frac{1}{n}.$$

Since $\|v_n^-\|_{L^2(Y^-)} = 1$ and $\|\nabla v_n^-\|_{L^2(Y^-)} \leq \|v_n\|_W \leq \dfrac{1}{n}$, v_n^- is bounded in $H^1(Y^-)$. Therefore it converges weakly in $H^1(Y^-)$. By compactness, we can extract a subsequence, still denoted v_n^-, such that v_n^- converges strongly in $L^2(Y^-)$. We denote by l its limit.

Besides, ∇v_n^- converges strongly to 0 in $L^2(Y^-)$. We thus have $\nabla l = 0$ and l constant in Y^-.

By applying in Y^+ the trace theorem and Poincaré–Wirtinger inequality to v_n^+, one also gets that

$$\|v_n^-\|_{L^2(\Gamma)} \leq \|v_n^+ - v_n^-\|_{L^2(\Gamma)} + \|v_n^+\|_{L^2(\Gamma)} \leq \|v_n^+ - v_n^-\|_{L^2(\Gamma)} + C\|v_n^+\|_{H^1(Y^+)} \leq \frac{C'}{n}.$$

Consequently, v_n^- converges strongly to 0 in $L^2(\Gamma)$ and $l = 0$ on Γ.

We have then $l = 0$ in Y^-, which leads to a contradiction. This proves (1.35).

We can now find an upper bound to (1.34):

$$\|v^-\|^2_{L^2(\Omega_\varepsilon^-)} \leq \varepsilon^2 C_1 \sum_{n \in N_\varepsilon} \int_{Y_n^+} |\nabla v_\varepsilon^+(y)|^2 dy + \int_{Y_n^-} |\nabla v_\varepsilon^-(y)|^2 dy + \int_{\Gamma_n} |v_\varepsilon^+(y) - v_\varepsilon^-(y)|^2 ds(y).$$

After the change of variable $x = \varepsilon y$, one gets

$$\|v^-\|^2_{L^2(\Omega_\varepsilon^-)} \leq \varepsilon C_1 \left(\|\nabla v^+\|^2_{L^2(\Omega_\varepsilon^+)} + \|\nabla v^-\|^2_{L^2(\Omega_\varepsilon^-)} + \varepsilon \|v^+ - v^-\|^2_{L^2(\Gamma_\varepsilon)} \right).$$

Since $\varepsilon < 1$, there exists a constant C_2, which does not depend on ε such that for every $v \in W_\varepsilon$,

$$\|v^-\|_{L^2(\Omega_\varepsilon^-)} \leq C_2 \|v\|_{W_\varepsilon},$$

which completes the proof. □

Theorem 1.3.2. *u_ε^- is uniformly bounded in ε in $H^1(\Omega_\varepsilon^-)$, i.e., there exists a constant C independent of ε, such that*

$$\|u_\varepsilon^-\|_{H^1(\Omega_\varepsilon^-)} \leq C.$$

Proof. By definition of the norm on W_ε, $\|\nabla u_\varepsilon^-\|^2_{L^2(\Omega_\varepsilon^-)} \leq \|u_\varepsilon\|^2_{W_\varepsilon}$.

We thus have with the result of Lemma 1.3.4:

$$\|u_\varepsilon^-\|^2_{H^1(\Omega_\varepsilon^-)} \leq C_1 \|u_\varepsilon\|^2_{W_\varepsilon}, \tag{1.36}$$

with a constant C_1 which does not depend on ε.

Furthermore, using the result of Theorem 1.3.1, there exists a constant C_2 independent of ε such that

$$|a(u_\varepsilon, u_\varepsilon)| \leq C_2.$$

We use the coercivity of a and get a uniform bound in ε of u_ε in W_ε. This bound and (1.36) complete the proof. □

Two-scale convergence

We first recall the definition of two-scale convergence and a few results of this theory [5].

Definition 1.3.1. *A sequence of functions u_ε in $L^2(\Omega)$ is said to* two-scale converge *to a limit u_0 belonging to $L^2(\Omega \times Y)$ if, for any function ψ in $L^2(\Omega, C_\sharp(Y))$, we have*

$$\lim_{\varepsilon \to 0} \int_\Omega u_\varepsilon(x) \psi(x, \frac{x}{\varepsilon}) dx = \int_\Omega \int_Y u_0(x,y) \psi(x,y) dx dy.$$

This notion of two-scale convergence makes sense because of the next compactness theorem.

Theorem 1.3.3. *From each bounded sequence u_ε in $L^2(\Omega)$, we can extract a subsequence, and there exists a limit $u_0 \in L^2(\Omega \times Y)$ such that this subsequence two-scale converges to u_0.*

Two-scale convergence can be extended to sequences defined on periodic surfaces.

Proposition 1.3.1. *For any sequence u_ε in $L^2(\Gamma_\varepsilon)$ such that*

$$\varepsilon \int_{\Gamma_\varepsilon} |u_\varepsilon|^2 dx \leq C, \tag{1.37}$$

there exists a subsequence, still denoted u_ε, and a limit function $u_0 \in L^2(\Omega, L^2(\Gamma))$ such that u_ε two-scale converges to u_0 in the sense

$$\lim_{\varepsilon\to 0} \varepsilon \int_{\Gamma_\varepsilon} u_\varepsilon(x)\psi(x,\frac{x}{\varepsilon})ds(x) = \int_\Omega \int_\Gamma u_0(x,y)\psi(x,y)dxds(y),$$

for any function $\psi \in L^2(\Omega, C_\sharp(Y))$.

Remark 1.3.1. *If u_ε and ∇u_ε are bounded in $L^2(\Omega)$, one can prove by using for example [7, Lemma 2.4.9] that u_ε verifies the uniform bound (1.37). The two-scale limit on the surface is then the trace on Γ of the two-scale limit of u_ε in Ω.*

In order to prove item (i) in Theorem 1.1.2, we need the following results.

Lemma 1.3.5. *Let the functions $(u_\varepsilon)_\varepsilon$ be the sequence of solutions of (1.2). There exist functions $u(x) \in H^1(\Omega)$, $v^+(x,y) \in L^2(\Omega, H^1_\sharp(Y^+))$ and $v^-(x,y) \in L^2(\Omega, H^1_\sharp(Y^-))$ such that, up to a subsequence,*

$$\begin{pmatrix} u_\varepsilon \\ \chi_\varepsilon^+(\frac{x}{\varepsilon})\nabla u_\varepsilon^+ \\ \chi_\varepsilon^-(\frac{x}{\varepsilon})\nabla u_\varepsilon^- \end{pmatrix} \quad \textit{two-scale converge to} \quad \begin{pmatrix} u(x) \\ \chi_{Y^+}(y)\Big(\nabla u(x) + \nabla_y v^+(x,y)\Big) \\ \chi_{Y^-}(y)\Big(\nabla u(x) + \nabla_y v^-(x,y)\Big) \end{pmatrix}.$$

Proof. We denote by $\tilde{\cdot}$ the extension by zero of functions on Ω_ε^+ and Ω_ε^- in the respective domains Ω_ε^- and Ω_ε^+.

From the previous estimates, $\widetilde{u}_\varepsilon^\pm$ and $\widetilde{\nabla u_\varepsilon}^\pm$ are bounded sequences in $L^2(\Omega)$. Up to a subsequence, they two-scale converge to $\tau^\pm(x,y)$ and $\xi^\pm(x,y)$. Since $\widetilde{u}_\varepsilon^\pm$ and $\widetilde{\nabla u_\varepsilon}^\pm$ vanish in $\Omega_\varepsilon^\mp$, so do $\tau^\pm$ and $\xi^\pm$.

Consider $\varphi \in \mathcal{D}(\Omega, C^\infty_\sharp(Y))^2$ such that $\varphi = 0$ for $y \in \overline{Y^-}$. By integrating by parts, it follows that

$$\varepsilon \int_{\Omega_\varepsilon^+} \nabla u_\varepsilon^+(x) \cdot \overline{\varphi}(x,\frac{x}{\varepsilon})dx = -\int_{\Omega_\varepsilon^+} u_\varepsilon^+(x) \left(\operatorname{div}_y \overline{\varphi}(x,\frac{x}{\varepsilon}) + \varepsilon \operatorname{div}_x \overline{\varphi}(x,\frac{x}{\varepsilon})\right) dx.$$

We take the limit of this equality as $\varepsilon \to 0$:

$$0 = -\int_{\Omega}\int_{Y^+} \tau^+(x,y)\mathrm{div}_y\,\overline{\varphi}(x,y)dxdy.$$

Therefore, τ^+ does not depend on y in Y^+, *i.e.*, there exists a function $u^+ \in L^2(\Omega)$ such that $\tau^+(x,y) = \chi_{Y^+}(y)u^+(x)$ for all $(x,y) \in \Omega \times Y$.

Take now $\varphi \in \mathcal{D}(\Omega, C^\infty_\sharp(Y))^2$ such that $\varphi = 0$ for $y \in \overline{Y^-}$ and $\mathrm{div}_y\varphi = 0$. Similarly, we have

$$\int_{\Omega_\varepsilon^+} \nabla u_\varepsilon^+(x) \cdot \overline{\varphi}(x, \frac{x}{\varepsilon})dx = -\int_{\Omega_\varepsilon^+} u_\varepsilon^+(x)\mathrm{div}_x\,\overline{\varphi}(x, \frac{x}{\varepsilon})dx,$$

and thus

$$\int_{\Omega}\int_{Y^+} \xi^+(x,y) \cdot \overline{\varphi}(x,y)dxdy = -\int_{\Omega}\int_{Y^+} u^+(x)\mathrm{div}_x\,\overline{\varphi}(x,y)dxdy. \tag{1.38}$$

For φ independent of y, this implies that $u^+ \in H^1(\Omega)$. Furthermore, if we integrate by parts the right-hand side of (1.38), we get

$$\int_{\Omega}\int_{Y^+} \xi^+(x,y) \cdot \overline{\varphi}(x,y)dxdy = \int_{\Omega}\int_{Y^+} \nabla u^+(x) \cdot \overline{\varphi}(x,y)dxdy,$$

for all $\varphi \in \mathcal{D}(\Omega, C^\infty_\sharp(Y^+))^2$ such that $\mathrm{div}_y\varphi = 0$ and $\varphi(x,y)\cdot n(y) = 0$ for y on Γ.

Since the orthogonal of the divergence-free functions are exactly the gradients, there exists a function $v^+ \in L^2(\Omega, H^1_\sharp(Y^+))$ such that

$$\xi^+(x,y) = \chi_{Y^+}(y)\left(\nabla u^+(x) + \nabla_y v^+(x,y)\right),$$

for all $(x,y) \in \Omega \times Y$.

Likewise, there exist functions $u^- \in H^1(\Omega)$ and $v^- \in L^2(\Omega, H^1_\sharp(Y^-))$ such that

$$\tau^-(x,y) = \chi_{Y^-}(y)u^-(x), \text{ and } \xi^-(x,y) = \chi_{Y^-}(y)\left(\nabla u^-(x) + \nabla_y v^-(x,y)\right),$$

for all $(x,y) \in \Omega \times Y$.

Furthermore, thanks to Remark 1.3.1, we have also

$$\varepsilon\int_{\Gamma_\varepsilon} u_\varepsilon^\pm(x)\overline{\varphi}(x, \frac{x}{\varepsilon})dx \xrightarrow[\varepsilon\to 0]{} \int_{\Omega}\int_{\Gamma} u^\pm(x,y)\overline{\varphi}(x,y)dxdy,$$

for all $\varphi \in L^2(\Omega, C^\infty_\sharp(\Gamma))$.

Recall that u_ε is a solution to the following variational form:

$$\int_{\Omega_\varepsilon^+} k_0\nabla u_\varepsilon^+(x)\cdot\nabla\overline{\varphi}_\varepsilon^+(x)dx + \int_{\Omega_\varepsilon^-} k_0\nabla u_\varepsilon^-(x)\cdot\nabla\overline{\varphi}_\varepsilon^-(x)dx$$
$$+\frac{1}{\varepsilon\beta}\int_{\Gamma_\varepsilon}\left(u_\varepsilon^+ - u_\varepsilon^-\right)\left(\overline{\varphi}_\varepsilon^+ - \overline{\varphi}_\varepsilon^-\right)ds - k_0\int_{\partial\Omega} g\overline{\varphi}_\varepsilon^+ ds = 0,$$

for all $(\varphi_\varepsilon^+, \varphi_\varepsilon^-) \in (H^1(\Omega_\varepsilon^+), H^1(\Omega_\varepsilon^-))$.

We multiply this equality by ε^2 and take the limit when ε goes to 0. The first two terms disappear and we obtain, for all $(\varphi^+, \varphi^-) \in \mathcal{D}(\Omega, C^\infty_\sharp(Y^+)) \times \mathcal{D}(\Omega, C^\infty_\sharp(Y^-))$:

$$\frac{1}{\beta}\int_\Omega \int_\Gamma (u^+(x) - u^-(x))(\overline{\varphi}^+(x,y) - \overline{\varphi}^-(x,y))dxdy = 0.$$

Thus $u^+(x) = u^-(x)$ for all $x \in \Omega$, and u_ε two-scale converges to $u = u^+ = u^- \in H^1(\Omega)$. This completes the proof. □

Now, we are ready to prove Theorem 1.1.2. For this, we need to show that u, v^+ and v^- are respectively u_0, solution of the homogenized problem (up to a constant), u_1^+ defined in (1.7) (up to a constant) and u_1^- defined in (1.7). The uniqueness of a solution for the homogenized problem and the cell problems will then allow us to conclude the convergence, not only up to a subsequence.

Proof. We first want to retrieve the expression of u_1 as a test function of the derivatives of u_0 and the cell problem solutions w_i.

We choose in the variational formulation (1.25) a function φ_ε of the form

$$\varphi_\varepsilon(x) = \varepsilon\varphi_1(x, \frac{x}{\varepsilon}),$$

where $\varphi_1 \in \mathcal{D}(\Omega, C^\infty_\sharp(Y^+)) \times \mathcal{D}(\Omega, C^\infty_\sharp(Y^-))$.

Lemma 1.3.5 shows the two-scale convergence of the following three terms:

$$\begin{aligned}
\int_{\Omega_\varepsilon^+} k_0 \nabla u_\varepsilon^+(x) \cdot \nabla \overline{\varphi}_\varepsilon^+(x)dx \quad &\underset{\varepsilon\to 0}{\longrightarrow} \quad \int_\Omega \int_{Y^+} k_0 \left(\nabla u(x) + \nabla_y v^+(x,y)\right) \cdot \nabla_y \overline{\varphi}_1^+(x,y)dxdy \\
\int_{\Omega_\varepsilon^-} k_0 \nabla u_\varepsilon^-(x) \cdot \nabla \overline{\varphi}_\varepsilon^-(x)dx \quad &\underset{\varepsilon\to 0}{\longrightarrow} \quad \int_\Omega \int_{Y^-} k_0 \left(\nabla u(x) + \nabla_y v^-(x,y)\right) \cdot \nabla_y \overline{\varphi}_1^-(x,y)dxdy \\
\int_{\partial\Omega} g(x)\overline{\varphi}_\varepsilon^+(x)ds(x) \quad &\underset{\varepsilon\to 0}{\longrightarrow} \quad 0.
\end{aligned}$$

We can not take directly the limit as $\varepsilon \to 0$ in the last term:

$$\begin{aligned}
&\frac{1}{\varepsilon\beta}\int_{\Gamma_\varepsilon} (u_\varepsilon^+(x) - u_\varepsilon^-(x))(\overline{\varphi}_\varepsilon^+(x) - \overline{\phi}_\varepsilon^-(x))ds(x) \\
&\qquad\qquad = \frac{1}{\beta}\int_{\Gamma_\varepsilon} (u_\varepsilon^+(x) - u_\varepsilon^-(x))\left(\overline{\varphi}_1^+(x,\frac{x}{\varepsilon}) - \overline{\varphi}_1^-(x,\frac{x}{\varepsilon})\right)ds(x).
\end{aligned}$$

Lemma A.4.1 ensures the existence of a function $\theta \in (\mathcal{D}(\Omega, H^1_\sharp(Y^+)) \times \mathcal{D}(\Omega, H^1_\sharp(Y^-)))^2$ such that for all $\psi \in H^1_\sharp(Y^+)/\mathbb{C} \times H^1_\sharp(Y^-)$:

$$\begin{aligned}
&\int_{Y^+} \nabla\psi^+(y) \cdot \overline{\theta}^+(x,y)dy + \int_{Y^-} \nabla\psi^-(y) \cdot \overline{\theta}^-(x,y)dy \\
&\qquad + \int_\Gamma \left(\psi^+(y) - \psi^-(y)\right)\left(\overline{\varphi}_1^+(x,y) - \overline{\varphi}_1^-(x,y)\right)ds(y) = 0.
\end{aligned} \tag{1.39}$$

We make the change of variables $y = \dfrac{x}{\varepsilon}$, sum over all $(Y_{\varepsilon,n})_{n\in N_\varepsilon}$, and choose $\psi = u_\varepsilon$ to get

$$\int_{\Gamma_\varepsilon} (u_\varepsilon^+(x) - u_\varepsilon^-(x)) \left(\overline{\varphi}_1^+(x, \frac{x}{\varepsilon}) - \overline{\varphi}_1^-(x, \frac{x}{\varepsilon})\right) ds(x) =$$
$$- \int_{\Omega_\varepsilon^+} \nabla u_\varepsilon^+(x, \frac{x}{\varepsilon}) \cdot \theta^+(x, \frac{x}{\varepsilon}) dx - \int_{\Omega_\varepsilon^-} \nabla u_\varepsilon^-(x, \frac{x}{\varepsilon}) \cdot \theta^-(x, \frac{x}{\varepsilon}) dx.$$

We can now take the limit as ε goes to 0:

$$\lim_{\varepsilon\to 0} \int_{\Gamma_\varepsilon} (u_\varepsilon^+(x) - u_\varepsilon^-(x)) \left(\overline{\varphi}_1^+(x, \frac{x}{\varepsilon}) - \overline{\varphi}_1^-(x, \frac{x}{\varepsilon})\right) ds(x) =$$
$$- \int_{Y^+} \left(\nabla u(x) + \nabla_y v^+(x,y)\right) \cdot \overline{\theta}^+(x,y) dxdy - \int_{Y^-} \left(\nabla u(x) + \nabla_y v^-(x,y)\right) \cdot \overline{\theta}^-(x,y) dxdy.$$

Finally, the variational formula (1.39) gives us

$$\lim_{\varepsilon\to 0} \int_{\Gamma_\varepsilon} (u_\varepsilon^+(x) - u_\varepsilon^-(x)) \left(\overline{\varphi}_1^+(x, \frac{x}{\varepsilon}) - \overline{\varphi}_1^-(x, \frac{x}{\varepsilon})\right) ds(x) =$$
$$\int_\Omega \int_\Gamma \left(v^+(y) - v^-(y)\right) \left(\overline{\varphi}_1^+(x,y) - \overline{\varphi}_1^-(x,y)\right) ds(y).$$

For $\varphi_\varepsilon(x) = \varepsilon\varphi_1(x, \dfrac{x}{\varepsilon})$, with $\varphi_1 \in \mathcal{D}(\Omega, C_\sharp^\infty(Y^+)) \times \mathcal{D}(\Omega, C_\sharp^\infty(Y^-))$, the two-scale limit of the variational formula is

$$\int_\Omega \int_{Y^+} k_0 \left(\nabla u(x) + \nabla_y v^+(x,y)\right) \cdot \nabla_y \overline{\varphi}_1^+(x,y) dxdy$$
$$+ \int_\Omega \int_{Y^-} k_0 \left(\nabla u(x) + \nabla_y v^-(x,y)\right) \cdot \nabla_y \overline{\varphi}_1^-(x,y) dxdy$$
$$+ \frac{1}{\beta} \int_\Omega \int_\Gamma \left(v^+(y) - v^-(y)\right) \left(\overline{\varphi}_1^+(x,y) - \overline{\varphi}_1^-(x,y)\right) ds(y) = 0.$$

By density, this formula hold true for $\varphi_1 \in L^2(\Omega, H_\sharp^1(Y^+)) \times L^2(\Omega, H_\sharp^1(Y^-))$. One can recognize the formula verified by $u_1^\pm$ and the definition of the cell problems. Hence, separation of variables and uniqueness of the solutions of the cell problems in W give

$$v^-(x,y) = u_1^- = \sum_{i=1,2} \frac{\partial u_0}{\partial x_i}(x) w_i^-(y)$$

and, up to a constant:

$$v^+(x,y) = u_1^+ = \sum_{i=1,2} \frac{\partial u_0}{\partial x_i}(x) w_i^+(y).$$

We now choose in the variational formula verified by u_ε a test function $\varphi_\varepsilon(x) = \varphi(x)$, with $\varphi \in C_c^\infty(\overline{\Omega})$.

The limit of (1.25) as ε goes to 0 is then given by

$$\int_\Omega \int_{Y^+} k_0 \left(\nabla u(x) + \nabla_y v^+(x,y) \right) \cdot \nabla \overline{\varphi}(x) dx dy$$
$$+ \int_\Omega \int_{Y^-} k_0 \left(\nabla u(x) + \nabla_y v^-(x,y) \right) \cdot \nabla \overline{\varphi}(x) dx dy$$
$$+ \int_{\partial\Omega} g(x) \overline{\phi}(x) ds(x) = 0.$$

By density, this formula hold true for $\varphi \in H^1(\Omega)$, which leads exactly to the variational formula of the homogenized problem (1.4). Since the solution of this problem is unique in $H^1_{\mathbb{C}}(\Omega)$, u_ε converges to u_0, not only up to a subsequence. Likewise, ∇u_ε two-scale converges to $\nabla u_0 + \chi_{Y^+} \nabla_y u_1^+ + \chi_{Y^-} \nabla_y u_1^-$. $\square$

Chapter 2

Effective admittivity for a dilute suspension and spectroscopic imaging

2.1 Effective admittivity for a dilute suspension

In general, the effective admittivity given by formula (1.5) can not be computed exactly except for a few configurations. In this section, we consider the problem of determining the effective property of a suspension of cells when the volume fraction $|Y^-|$ goes to zero. In other words, the cells have much less volume than the medium surrounding them. This kind of suspension is called dilute. Many approximations for the effective properties of composites are based on the solution for dilute suspension.

2.1.1 Computation of the effective admittivity

We investigate the periodic double-layer potential used in calculating effective permittivity of a suspension of cells. We introduce the periodic Green function $G_\sharp$, for the Laplace equation in Y, given by

$$\forall x \in Y, \qquad G_\sharp(x) = \sum_{n \in \mathbb{Z}^2 \setminus \{0\}} \frac{e^{i2\pi n \cdot x}}{4\pi^2 |n|^2}.$$

The following lemma from [32, 29] plays an essential role in deriving the effective properties of a suspension in the dilute limit.

Lemma 2.1.1. *The periodic Green function $G_\sharp$ admits the following decomposition:*

$$\forall x \in Y, \qquad G_\sharp(x) = \frac{1}{2\pi} \ln |x| + R_2(x), \tag{2.1}$$

where R_2 is a smooth function with the following Taylor expansion at 0:

$$R_2(x) = R_2(0) - \frac{1}{4}(x_1^2 + x_2^2) + O(|x|^4). \tag{2.2}$$

Let $L^2_0(\Gamma) := \left\{ \varphi \in L^2(\Gamma) \Big| \int_\Gamma \varphi(x) ds(x) = 0 \right\}$.

We define the periodic double-layer potential $\widetilde{\mathcal{D}}_\Gamma$ of the density function $\varphi \in L^2_0(\Gamma)$:

$$\widetilde{\mathcal{D}}_\Gamma[\varphi](x) = \int_\Gamma \frac{\partial}{\partial n_y} G_\sharp(x-y)\varphi(y) ds(y).$$

The double-layer potential has the following properties [29].

Lemma 2.1.2. *Let $\varphi \in L^2_0(\Gamma)$. $\widetilde{\mathcal{D}}_\Gamma[\varphi]$ verifies:*

$$\begin{aligned}
&(i) && \Delta \widetilde{\mathcal{D}}_\Gamma[\varphi] = 0 && \text{in } Y^+,\\
& && \Delta \widetilde{\mathcal{D}}_\Gamma[\varphi] = 0 && \text{in } Y^-,\\
&(ii) && \frac{\partial}{\partial n}\widetilde{\mathcal{D}}_\Gamma[\varphi]\Big|_+ = \frac{\partial}{\partial n}\widetilde{\mathcal{D}}_\Gamma[\varphi]\Big|_- && \text{on } \Gamma,\\
&(iii) && \widetilde{\mathcal{D}}_\Gamma[\varphi]\Big|_\pm = \left(\mp\frac{1}{2}I + \widetilde{\mathcal{K}}_\Gamma\right)[\varphi] && \text{on } \Gamma,
\end{aligned}$$

where $\widetilde{\mathcal{K}}_\Gamma : L^2_0(\Gamma) \mapsto L^2_0(\Gamma)$ is the Neumann–Poincaré operator defined by

$$\forall x \in \Gamma, \qquad \widetilde{\mathcal{K}}_\Gamma[\varphi](x) = \int_\Gamma \frac{\partial}{\partial n_y} G_\sharp(x-y)\varphi(y) ds(y).$$

The following integral representation formula holds.

Theorem 2.1.1. *Let w_i be the unique solution in W of (1.6) for $i = 1, 2$. w_i admits the following integral representation in Y:*

$$w_i = -\beta k_0 \widetilde{\mathcal{D}}_\Gamma \left(I + \beta k_0 \widetilde{\mathcal{L}}_\Gamma\right)^{-1}[n_i], \tag{2.3}$$

where $\widetilde{\mathcal{L}}_\Gamma = \dfrac{\partial \widetilde{\mathcal{D}}_\Gamma}{\partial n}$ and $n = (n_i)_{i=1,2}$ is the outward unit normal to Γ.

Proof. Let $\varphi := -\beta k_0 \left(I + \beta k_0 \widetilde{\mathcal{L}}\right)^{-1}[n_i]$. φ verifies :

$$\int_\Gamma \varphi(y) ds(y) = -\beta k_0 \int_\Gamma \frac{\partial}{\partial n}(\widetilde{\mathcal{D}}_\Gamma[\varphi](y) + y_i) ds(y) = 0.$$

The first equality comes from the definition of φ and the second from an integration by parts and the fact that $\widetilde{\mathcal{D}}_\Gamma[\varphi]$ and I are harmonic. Consequently, $\varphi \in L^2_0(\Gamma)$.

We now introduce $V_i := \widetilde{\mathcal{D}}_\Gamma[\varphi]$. V_i is solution to the following problem:

$$\begin{cases}
\nabla \cdot k_0 \nabla V_i = 0 & \text{in } Y^+,\\
\nabla \cdot k_0 \nabla V_i = 0 & \text{in } Y^-,\\
k_0 \dfrac{\partial V_i}{\partial n}\Big|_+ = k_0 \dfrac{\partial V_i}{\partial n}\Big|_- & \text{on } \Gamma,\\
V_i|_+ - V_i|_- = \varphi & \text{on } \Gamma,\\
y \longmapsto V_i(y) \ Y\text{-periodic.}
\end{cases}$$

We use the definitions of φ and V_i and recognize that the last problem is exactly problem (1.6). The uniqueness of the solution in W gives us the wanted result. $\square$

From Theorem 1.1.2, the effective admittivity of the medium K^* is given by

$$\forall (i,j) \in \{1,2\}^2, \qquad K^*_{i,j} = k_0 \left(\delta_{ij} + \int_Y \nabla w_i \cdot e_j \right).$$

After an integration by parts, we get

$$\forall (i,j) \in \{1,2\}^2, \qquad K^*_{i,j} = k_0 \left(\delta_{ij} + \int_{\partial Y} w_i(y) n_j(y)\, ds(y) - \int_\Gamma \left(w_i^+ - w_i^- \right) n_j(y)\, ds(y) \right).$$

Because of the Y-periodicity of w_i, we have: $\displaystyle\int_{\partial Y} w_i(y) n_j\, ds(y) = 0$.

Finally, the integral representation 2.3 gives us that

$$\forall (i,j) \in \{1,2\}^2, \qquad K^*_{i,j} = k_0 \left(\delta_{ij} - (\beta k_0) \int_\Gamma \left(I + \beta k_0 \widetilde{\mathcal{L}}_\Gamma \right)^{-1} [n_i] n_j\, ds(y) \right).$$

We consider that we are in the context of a dilute suspension, *i.e.*, the size of the cell is small compared to the square: $\left|Y^-\right| \ll |Y| = 1$. We perform the change of variable: $z = \rho^{-1} y$ with $\rho = |Y^-|^{\frac{1}{2}}$ and obtain that

$$\forall (i,j) \in \{1,2\}^2, \qquad K^*_{i,j} = k_0 \left(\delta_{ij} - \rho^2 (\beta k_0) \int_{\rho^{-1}\Gamma} \left(I + \rho\beta k_0 \widetilde{\mathcal{L}}_\Gamma \right)^{-1} [n_i](\rho z) n_j(z)\, ds(z) \right),$$

where n is the outward unit normal to Γ. Note that, in the same way as before, β becomes $\rho\beta$ when we rescale the cell.

Let us introduce $\varphi_i = -\left(I + \rho\beta k_0 \widetilde{\mathcal{L}}_\Gamma \right)^{-1} [n_i]$ and $\psi_i(z) = \varphi_i(\rho z)$ for all $z \in \rho^{-1}\Gamma$. From (2.1), we get, for any $z \in \rho^{-1}\Gamma$, after changes of variable in the integrals:

$$\widetilde{\mathcal{L}}_\Gamma[\varphi_i](\rho z) = \frac{\partial}{\partial n} \widetilde{\mathcal{D}}_\Gamma[\varphi_i](\rho z) = \rho^{-1} \frac{\partial}{\partial n} \mathcal{D}_{\rho^{-1}\Gamma}[\psi_i](z) + \frac{\partial}{\partial n(z)} \int_{\rho^{-1}\Gamma} \frac{\partial}{\partial n(y)} R_2(\rho z - \rho y) \varphi(\rho y) ds(y).$$

Besides, the expansion (2.2) gives us that the estimate

$$\nabla R_2(\rho(z-y)) \cdot n(y) = -\frac{\rho}{2}(z-y) \cdot n(y) + O(\rho^3),$$

holds uniformly in $z, y \in \rho^{-1}\Gamma$.

We thus get the following expansion:

$$\widetilde{\mathcal{L}}_\Gamma[\varphi_i](\rho z) = \rho^{-1} \mathcal{L}_{\rho^{-1}\Gamma}[\psi_i](z) - \frac{\rho}{2} \sum_{j=1,2} n_j \int_{\rho^{-1}\Gamma} n_j \psi_i(y) ds(y) + O(\rho^4).$$

Using ψ_i^* defined by (1.11) we get on $\rho^{-1}\Gamma$:

$$\psi_i = \psi_i^* + \beta k_0 \frac{\rho^2}{2} \sum_{j=1,2} \psi_j^* \int_{\rho^{-1}\Gamma} n_j(y) \psi_i(y) ds(y) + O(\rho^4). \tag{2.4}$$

By iterating the formula (2.4), we obtain on $\rho^{-1}\Gamma$ that

$$\psi_i = \psi_i^* + \beta k_0 \frac{\rho^2}{2} \sum_{j=1,2} \psi_j^* \int_{\rho^{-1}\Gamma} n_j(y) \psi_i^*(y) ds(y) + O(\rho^4).$$

Therefore, one can easily see that Theorem 1.1.3 holds.

2.1.2 Case of concentric circular-shaped cells: the Maxwell-Wagner-Fricke formula

We consider in this section that the cells are disks of radius r_0. $\rho^{-1}\Gamma$ becomes a circle of radius r_0.

For all $g \in L^2((0,2\pi))$, we introduce the Fourier coefficients:

$$\forall m \in \mathbb{Z}, \quad \hat{g}(m) = \frac{1}{2\pi}\int_0^{2\pi} g(\varphi)e^{-im\varphi}d\varphi,$$

and have then for all $\varphi \in (0,2\pi)$:

$$g(\varphi) = \sum_{m=-\infty}^{\infty} \hat{g}(m)e^{im\varphi}.$$

For $f \in \mathcal{C}^{2,\eta}(\rho^{-1}\Gamma)$, we obtain after a few computations:

$$\forall \theta \in]0,2\pi[, \quad (I+\beta k_0 \mathcal{L}_{\rho^{-1}\Gamma})^{-1}[f](\theta) = \sum_{n\in\mathbb{Z}^*}\left(1+\beta k_0 \frac{|n|}{2r_0}\right)^{-1}\hat{f}(n)\, e^{in\theta}.$$

For $p=1,2$, $\psi_p^* = -(I+\beta k_0 \mathcal{L}_{\rho^{-1}\Gamma})^{-1}[n_p]$ then have the following expression:

$$\forall \theta \in (0,2\pi), \quad \psi_p^* = -\left(1+\frac{\beta k_0}{2r_0}\right)^{-1} n_p.$$

Consequently, we get for $(p,q) \in \{1,2\}^2$:

$$M_{p,q} = -\delta_{pq}\frac{\beta k_0 \pi r_0}{1+\dfrac{\beta k_0}{2r_0}},$$

and hence,

$$\Im M_{p,q} = \delta_{p,q}\frac{\pi r_0 \delta \omega(\epsilon_m \sigma_0 - \epsilon_0 \sigma_m)}{(\sigma_m + \sigma_0\dfrac{\delta}{2r_0})^2 + \omega^2(\epsilon_m + \epsilon_0\dfrac{\delta}{2r_0})^2}. \tag{2.5}$$

Formula (2.5) is the two-dimensional version of the Maxwell-Wagner-Fricke formula, which gives the effective admittivity of a dilute suspension of spherical cells covered by a thin membrane.

An explicit formula for the case of elliptic cells can be derived by using the spectrum of the integral operator $\mathcal{L}_{\rho^{-1}\Gamma}$, which can be identified by standard Fourier methods [76].

2.1.3 Debye relaxation times

From (2.5), it follows that the imaginary part of the membrane polarization attains its maximum with respect to the frequency at

$$\frac{1}{\tau} = \frac{\sigma_m + \sigma_0\dfrac{\delta}{2r_0}}{\epsilon_m + \epsilon_0\dfrac{\delta}{2r_0}}.$$

This dispersion phenomenon due to the membrane polarization is well known and referred to as the β-dispersion. The associated characteristic time τ corresponds to a Debye relaxation time.

For arbitrary-shaped cells, we define the first and second Debye relaxation times, $\tau_i, i = 1, 2$, by

$$\frac{1}{\tau_i} := \arg\max_{\omega} |\lambda_i(\omega)|, \tag{2.6}$$

where $\lambda_1 \leq \lambda_2$ are the eigenvalues of the imaginary part of the membrane polarization tensor $M(\omega)$. Note that if the cell is of circular shape, $\lambda_1 = \lambda_2$.

As it will be shown later, the Debye relaxation times can be used for identifying the microstructure.

2.1.4 Properties of the membrane polarization tensor and the Debye relaxation times

In this subsection, we derive important properties of the membrane polarization tensor and the Debye relaxation times defined respectively by (1.10) and (2.6). In particular, we prove that the Debye relaxation times are invariant with respect to translation, scaling, and rotation of the cell.

First, since the kernel of $\mathcal{L}_{\rho^{-1}\Gamma}$ is invariant with respect to translation, it follows that $M(C, \beta k_0)$ is invariant with respect to translation of the cell C.

Next, from the scaling properties of the kernel of $\mathcal{L}_{\rho^{-1}\Gamma}$ we have

$$M(sC, \beta k_0) = s^2 M(C, \frac{\beta k_0}{s})$$

for any scaling parameter $s > 0$.

Finally, we have

$$M(\mathcal{R}C, \beta k_0) = \mathcal{R} M(C, \beta k_0) \mathcal{R}^t \quad \text{for any rotation } \mathcal{R},$$

where t denotes the transpose.

Therefore, the Debye relaxation times are translation and rotation invariant. Moreover, for scaling, we have

$$\tau_i(hC, \beta k_0) = \tau_i(C, \frac{\beta k_0}{h}), \qquad i = 1, 2, \quad h > 0.$$

Since β is proportional to the thickness of the cell membrane, β/h is nothing else than the real rescaled coefficient β for the cell C. The Debye relaxation times (τ_i) are therefore invariant by scaling.

Since $\mathcal{L}_{\rho^{-1}\Gamma}$ is self-adjoint, it follows that M is symmetric. Finally, we show positivity of the imaginary part of the matrix M for δ small enough.

We consider that the cell contour Γ can be parametrized by polar coordinates. We have, up to $O(\delta^3)$,

$$M + \beta\rho^{-1}|\Gamma| = -\beta^2 \int_{\rho^{-1}\Gamma} n \mathcal{L}_{\rho^{-1}\Gamma}[n]\, ds, \tag{2.7}$$

where again we have assumed that $\sigma_0 = 1$ and $\epsilon_0 = 0$.

Recall that
$$\beta = \frac{\delta\sigma_m}{\sigma_m^2 + \omega^2\varepsilon_m^2} - i\frac{\delta\omega\varepsilon_m}{\sigma_m^2 + \omega^2\varepsilon_m^2}.$$
Hence, the positivity of $\mathcal{L}_{\rho^{-1}\Gamma}$ yields
$$\Im M \geq \frac{\delta\omega\varepsilon_m}{2\rho(\sigma_m^2 + \omega^2\varepsilon_m^2)}|\Gamma| I$$
for δ small enough, where I is the identity matrix.

Finally, by using (2.7) one can see that the eigenvalues of $\Im M$ have one maximum each with respect to the frequency. Let $l_i, i = 1,2$, $l_1 \geq l_2$, be the eigenvalues of $\int_{\rho^{-1}\Gamma} n\mathcal{L}_{\rho^{-1}\Gamma}[n]ds$. We have
$$\lambda_i = \frac{\delta\omega\varepsilon_m}{\rho(\sigma_m^2 + \omega^2\varepsilon_m^2)}|\Gamma| - \frac{2\delta^2\omega\varepsilon_m\sigma_m}{(\sigma_m^2 + \omega^2\varepsilon_m^2)^2} l_i, \quad i = 1,2. \tag{2.8}$$
Therefore, τ_i is the inverse of the positive root of the following polynomial in ω:
$$-\varepsilon_m^4|\Gamma|\omega^4 + 6\delta\varepsilon_m^2\sigma_m l_i\rho\omega^2 + \sigma_m^4|\Gamma|.$$

2.1.5 Anisotropy measure

Anisotropic electrical properties can be found in biological tissues such as muscles and nerves. In this subsection, based on formula (1.9), we introduce a natural measure of the conductivity anisotropy and derive its dependence on the frequency of applied current. Assessment of electrical anisotropy of muscle may have useful clinical application. Because neuromuscular diseases produce substantial pathological changes, the anisotropic pattern of the muscle is likely to be highly disturbed [47, 62]. Neuromuscular diseases could lead to a reduction in anisotropy for a range of frequencies as the muscle fibers are replaced by isotropic tissue.

Let $\lambda_1 \leq \lambda_2$ be the eigenvalues of the imaginary part of the membrane polarization tensor $M(\omega)$. The function
$$\omega \mapsto \frac{\lambda_1(\omega)}{\lambda_2(\omega)}$$
can be used as a measure of the anisotropy of the conductivity of a dilute suspension. Assume $\epsilon_0 = 0$. As frequency ω increases, the factor βk_0 decreases. Therefore, for large ω, using the expansions in (2.8) we obtain that
$$\frac{\lambda_1(\omega)}{\lambda_2(\omega)} = 1 + (l_1 - l_2)\frac{2\delta\sigma_m\rho}{(\sigma_m^2 + \omega^2\varepsilon_m^2)|\Gamma|} + O(\delta^2), \tag{2.9}$$
where $l_1 \leq l_2$ are the eigenvalues of $\int_{\rho^{-1}\Gamma} n\mathcal{L}_{\rho^{-1}\Gamma}[n]ds$.

Formula (2.9) shows that as the frequency increases, the conductivity anisotropy decreases. The anisotropic information can not be captured for
$$\omega \gg \frac{1}{\varepsilon_m}((l_1 - l_2)\frac{2\delta\sigma_m\rho}{|\Gamma|} - \sigma_m^2)^{1/2}.$$

2.2 Spectroscopic imaging of a dilute suspension

2.2.1 Spectroscopic conductivity imaging

We now make use of the asymptotic expansion of the effective admittivity in terms of the volume fraction $f = \rho^2$ to image a permittivity inclusion. Consider D to be a bounded domain in Ω with admittivity $1 + fM(\omega)$, where $M(\omega)$ is a membrane polarization tensor and f is the volume fraction of the suspension in D. The inclusion D models a suspension of cells in the background Ω. For simplicity, we neglect the permittivity ϵ_0 of Ω and assume that its conductivity $\sigma_0 = 1$. We also assume that $M(\omega)$ is isotropic. At the macroscopic scale, if we inject a current g on $\partial\Omega$, then the electric potential satisfies:

$$\begin{cases} \nabla \cdot (1 + fM(\omega)\chi_D)\nabla u = 0 & \text{in } \Omega, \\ \left.\dfrac{\partial u}{\partial n}\right|_{\partial\Omega} = g, \quad \displaystyle\int_{\partial\Omega} g(x)ds(x) = 0, \quad \int_\Omega u(x)dx = 0. & \end{cases} \tag{2.10}$$

The imaging problem is to detect and characterize D from measurements of u on $\partial\Omega$.

Integrating by parts and using the trace theorem for the double-layer potential [49, 102], we obtain, $\forall\, x \in \partial\Omega$,

$$\begin{aligned} &\frac{1}{2}u(x) + \frac{1}{2\pi}\int_{\partial\Omega} \frac{(x-y)\cdot n(x)}{|x-y|^2}u(y)ds(y) + \frac{1}{2\pi}\int_{\partial\Omega} g(y)\ln|x-y|ds(y) \\ &\quad = \frac{f}{2\pi}M(\omega)\int_D \nabla u(y)\cdot\frac{(x-y)}{|x-y|^2}dy. \end{aligned} \tag{2.11}$$

Since f is small,

$$\int_D \nabla u(y)\cdot\frac{(x-y)}{|x-y|^2}dy \simeq \int_D \nabla U(y)\cdot\frac{(x-y)}{|x-y|^2}dy$$

holds uniformly for $x \in \partial\Omega$, where U is the background solution, that is,

$$\begin{cases} \Delta U = 0 & \text{in } \Omega, \\ \left.\dfrac{\partial U}{\partial n}\right|_{\partial\Omega} = g, \quad \displaystyle\int_\Omega U(x)dx = 0. & \end{cases}$$

Therefore, taking the imaginary part of (2.11) yields

$$\frac{1}{2}\Im u(x) + \frac{1}{2\pi}\int_{\partial\Omega}\frac{(x-y)\cdot n(x)}{|x-y|^2}\Im u(y)ds(y) \simeq \frac{f}{2\pi}\Im M(\omega)\int_D \nabla U(y)\cdot\frac{(x-y)}{|x-y|^2}dy, \tag{2.12}$$

uniformly for $x \in \partial\Omega$, provided that g is real. Finally, taking the argument of the maximum of the right-hand side in (2.12) with respect to the frequency ω gives the Debye relaxation time of the suspension in D.

2.2.2 Selective spectroscopic imaging

A challenging applied problem is to design a selective spectroscopic imaging approach for suspensions of cells. Using a pulsed imaging approach [71, 78], we propose a simple way to selectively image dilute suspensions. Again, we assume for the sake of simplicity that $\epsilon_0 = 0$ and $\sigma_0 = 1$.

In the time-dependant regime, the electrical model for the cell (1.1) is replaced with

$$u(x,t) = \int \hat{h}(\omega)\hat{u}(x,\omega)e^{i\omega t}d\omega,$$

where $\hat{u}(x,\omega)$ is the solution to

$$\begin{cases} \Delta\hat{u}(\cdot,\omega) = 0 & \text{in } D \setminus \overline{C}, \\ \Delta\hat{u}(\cdot,\omega) = 0 & \text{in } C, \\ \dfrac{\partial\hat{u}(\cdot,\omega)}{\partial n}\Big|_+ = \dfrac{\partial\hat{u}(\cdot,\omega)}{\partial n}\Big|_- & \text{on } \Gamma, \\ \hat{u}(\cdot,\omega)|_+ - \hat{u}(\cdot,\omega)|_- - \beta(\omega)\dfrac{\partial\hat{u}(\cdot,\omega)}{\partial n} = 0 & \text{on } \Gamma, \\ \dfrac{\partial\hat{u}(\cdot,\omega)}{\partial n}\Big|_{\partial D} = f, \quad \displaystyle\int_{\partial D}\hat{u}(\cdot,\omega)ds = 0, & \end{cases} \tag{2.13}$$

and

$$h(t) = \int \hat{h}(\omega)e^{i\omega t}d\omega$$

is the pulse shape. The support of h is assumed to be compact.

At the macroscopic scale, if we inject a pulsed current, $g(x)h(t)$, on $\partial\Omega$, then the electric potential $u(x,t)$ in the presence of a suspension occupying D is given by

$$u(x,t) = \int \hat{h}(\omega)\hat{u}(x,\omega)e^{i\omega t}d\omega,$$

where

$$\begin{cases} \nabla\cdot(1 + fM(\omega)\chi_D)\nabla\hat{u}(\cdot,\omega) = 0 & \text{in } \Omega, \\ \dfrac{\partial\hat{u}(\cdot,\omega)}{\partial n}\Big|_{\partial\Omega} = g, \quad \displaystyle\int_{\partial\Omega}\hat{u}(\cdot,\omega)ds = 0. & \end{cases}$$

Assume that we are in the presence of two suspensions occupying the domains D_1 and D_2 inside Ω. From (2.11) it follows that

$$\begin{aligned} &\frac{1}{2}\hat{u}(x,\omega) + \frac{1}{2\pi}\int_{\partial\Omega}\frac{(x-y)\cdot n(x)}{|x-y|^2}\hat{u}(y,\omega)ds(y) + \frac{1}{2\pi}\int_{\partial\Omega}g(y)\ln|x-y|ds(y) \\ &\quad\simeq \frac{f_1}{2\pi}M_1(\omega)\int_{D_1}\nabla U(y)\cdot\frac{(x-y)}{|x-y|^2}dy + \frac{f_2}{2\pi}M_2(\omega)\int_{D_2}\nabla U(y)\cdot\frac{(x-y)}{|x-y|^2}dy, \end{aligned} \tag{2.14}$$

and therefore,

$$\begin{aligned}\frac{1}{2}u(x,t) + \frac{1}{2\pi}\int_{\partial\Omega}\frac{(x-y)\cdot n(x)}{|x-y|^2}u(y,t)ds(y) + \frac{1}{2\pi}h(t)\int_{\partial\Omega}g(y)\ln|x-y|ds(y)\\ \simeq \frac{f_1}{2\pi}\mathcal{M}_1(t)\int_{D_1}\nabla U(y)\cdot\frac{(x-y)}{|x-y|^2}dy + \frac{f_2}{2\pi}\mathcal{M}_2(t)\int_{D_2}\nabla U(y)\cdot\frac{(x-y)}{|x-y|^2}dy,\end{aligned} \tag{2.15}$$

uniformly in $x \in \partial\Omega$ and $t \in \operatorname{supp} h$, where

$$\mathcal{M}_i(t) := \int \hat{h}(\omega)M_i(\omega)e^{i\omega t}d\omega, \quad i = 1, 2.$$

As it will be shown in chapter 4, by comparing the Debye relaxation times associated to M_1 and M_2, one can design the pulse shape h in order to image selectively D_1 or D_2. For example, one can selectively image D_1 by taking $\hat{h}(\omega)$ close to zero around the Debye relaxation time of M_2 and close to one around the Debye relaxation time of M_1.

2.2.3 Spectroscopic measurement of anisotropy

In this subsection we assume that M is anisotropic and consider the solution u to (2.10). We want to assess the anisotropy of the inclusion D of admittivity $1 + fM(\omega)$ from measurements of u on the boundary $\partial\Omega$.

From (2.12) it follows that

$$\begin{aligned}\int_{\partial\Omega}g(x)\left[\frac{1}{2}\Im u(x) + \frac{1}{2\pi}\int_{\partial\Omega}\frac{(x-y)\cdot n(x)}{|x-y|^2}\Im u(y)ds(y)\right]ds(x)\\ \simeq \frac{f}{2\pi}\int_D \Im M(\omega)\nabla U(y)\cdot\nabla U(y)dy,\end{aligned} \tag{2.16}$$

provided that g is real. Now, taking constant current sources corresponding to $g = a \cdot n$, where $a \in \mathbb{R}^2$ is a unit vector, yields

$$\mathcal{S}[a] := \int_{\partial\Omega}g(x)\left[\frac{1}{2}\Im u(x) + \frac{1}{2\pi}\int_{\partial\Omega}\frac{(x-y)\cdot n(x)}{|x-y|^2}\Im u(y)ds(y)\right]ds(x) \simeq \frac{f}{2\pi}\Im M(\omega)|a|^2|D|.$$

Since

$$\frac{\min_a \mathcal{S}[a]}{\max_a \mathcal{S}[a]} \simeq \frac{\lambda_1(\omega)}{\lambda_2(\omega)},$$

where λ_1 and λ_2 (with $\lambda_1 \leq \lambda_2$) are the eigenvalues of $\Im M$, it follows from subsection 2.1.5 that

$$\omega \mapsto \frac{\min_a \mathcal{S}[a]}{\max_a \mathcal{S}[a]}$$

is a natural measure of conductivity anisotropy. This measure may be used for the detection and classification of neuromuscular diseases via measurement of muscle anisotropy [47, 62].

Chapter 3

Stochastic homogenization of randomly deformed membranes

The first main result of this section is to show that a rigorous homogenization theory can be derived when the cells (and hence interfaces) are randomly deformed from a periodic structure, and the random deformation is ergodic and stationary in the sense of (1.12).

3.1 Auxiliary problem: proof of Theorem 1.1.4

In this subsection, we prove Theorem 1.1.4 about the existence and uniqueness of the auxiliary problem. This is the key step in stochastic homogenization. The main difficulty is due to the fact that one does not have compactness in the general stationary ergodic setting.

We first make the weak formulation of the system (1.19) precise. To this end, we introduce the space $\widetilde{\mathcal{H}} := L^2(\mathcal{O}, H^1_{\mathrm{loc}}(\mathbb{R}_2^+) \times H^1_{\mathrm{loc}}(\mathbb{R}_2^-))$ and the space $\widetilde{\mathcal{H}}_S$ which is a subspace of $\widetilde{\mathcal{H}}$ where the elements are stationary. Define also the space $\mathcal{H} := \{w = \widetilde{w} \circ \Phi^{-1} \mid \widetilde{w} \in \widetilde{\mathcal{H}}\}$ and the space $\mathcal{H}_S := \{w = \widetilde{w} \circ \Phi^{-1} \mid \widetilde{w} \in \widetilde{\mathcal{H}}_S\}$.

We say that $w_p = w_p^+ \chi_{\Phi(\mathbb{R}_2^+)} + w_p^- \chi_{\Phi(\mathbb{R}_2^-)} \in \mathcal{H}$ is a weak solution to (1.19) if ∇w_p is stationary and for all $\varphi \in \mathcal{H}$ with compact support $K \subset \mathbb{R}^2$, it holds that

$$\begin{aligned}\mathbb{E} \int_{K \cap \Phi(\mathbb{R}_2^+, \gamma)} k_0 (p + \nabla w_p^+) \cdot \nabla \overline{\varphi} dx + \mathbb{E} \int_{K \cap \Phi(\mathbb{R}_2^-, \gamma)} k_0 (p + \nabla w_p^-) \cdot \nabla \overline{\varphi} dx \\ + \mathbb{E} \int_{K \cap \Phi(\Gamma, \gamma)} \frac{1}{\beta} (w_p^+ - w_p^- - \beta k_0 p)(\overline{\varphi}^+ - \overline{\varphi}^-) ds(x) = 0.\end{aligned} \tag{3.1}$$

Since the integrals above does not control $\|w_p^\pm\|_{L^2(\Omega, L^2_{\mathrm{loc}}(\Phi(\mathbb{R}_2^\pm)))}$ and the space $\mathcal{H}$ does not possess Poincaré inequality, the existence of weak solutions is not immediate.

Our strategy which is standard is as follows: First, an absorption term is added to regularize the problem. The sequence of regularized solutions, which correspond to a sequence of vanishing regularization, have a converging gradient. Secondly, the potential field corresponds to the limiting gradient is shown to be a solution to the auxiliary problem. Finally, using regularity results and sub-linear growth of potential field with stationary gradient, we prove that the gradient of the solution to the auxiliary problem is unique.

Proof of Theorem 1.1.4. Step 1: The regularized auxiliary problem. Fix $p \in \mathbb{R}^2$. Consider the following regularized problem where an absorption $\alpha > 0$ is added.

$$\begin{cases} -\nabla \cdot k_0(\nabla w^{\pm}_{p,\alpha}(y) + p) + \alpha w^{\pm}_{p,\alpha} = 0 & \text{in} \quad \Phi(\mathbb{R}^{\pm}_2, \gamma), \\ n \cdot k_0 \nabla w^{-}_{p,\alpha}(y) = n \cdot k_0 \nabla w^{-}_{p,\alpha}(y), & \text{in} \quad \Phi(\Gamma_2, \gamma), \\ w^{+}_{p,\alpha} - w^{-}_{p,\alpha} = \beta k_0 n \cdot (\nabla w^{-}_{p,\alpha} + p) & \text{in} \quad \Phi(\Gamma_2, \gamma), \\ w^{\pm}_{p,\alpha}(y,\gamma) = \widetilde{w}^{\pm}_{p,\alpha}(\Phi^{-1}(y,\gamma),\gamma), & \text{and} \quad \widetilde{w}^{\pm}_{p,\alpha} \text{ are stationary.} \end{cases} \tag{3.2}$$

We first construct a solution for the above equation in $\mathcal{H}_S$ in a sense weaker than (3.1) as follows. It can be verified that $\mathcal{H}_S$ equipped with the inner product

$$(u,v)_{\mathcal{H}_S} = \mathbb{E}\left(\int_{Y^+} \nabla\tilde{u} \cdot \nabla\overline{\tilde{v}} dx + \int_{Y^-} \nabla\tilde{u} \cdot \nabla\overline{\tilde{v}} dx + \int_Y \tilde{u}\overline{\tilde{v}} dx\right).$$

is a Hilbert space. For any fixed $\alpha > 0$, define the bilinear form $A_\alpha : \mathcal{H}_S \times \mathcal{H}_S \to \mathbb{R}$ by

$$\begin{aligned} A_\alpha(u,v) = \mathbb{E}\Bigg(&\int_{\Phi(Y^+)} k_0 \nabla u^+ \cdot \overline{\nabla v^+} dx + \int_{\Phi(Y^-)} k_0 \nabla u^- \cdot \overline{\nabla v^-} dx \\ &+ \alpha \int_{\Phi(Y)} u\overline{v} dx + \frac{1}{\beta}\int_{\Phi(\Gamma_0)} (u^+ - u^-)\overline{(v^+ - v^-)} ds\Bigg), \end{aligned}$$

and the linear functional $b_p : \mathcal{H}_S \to \mathbb{R}$ by

$$b_p(v) = -k_0 \mathbb{E}\left(\int_{\Phi(Y^+)} p \cdot \overline{\nabla v^+} dx + \int_{\Phi(Y^-)} p \cdot \overline{\nabla v^-} dx + \int_{\Phi(\Gamma_0)} (n(x)\cdot p)\overline{(v^+ - v^-)}(x) ds(x)\right).$$

We verify that A_α is bounded and coercive, and b_p is bounded. By the Lax–Milgram theorem, there exists a unique element $w_{p,\alpha} \in \mathcal{H}_S$ satisfying

$$A_\alpha(w_{p,\alpha}, \varphi) = b_p(\varphi), \quad \forall \varphi \in \mathcal{H}_S. \tag{3.3}$$

By choosing φ to be $w_{p,\alpha}$, we obtain the estimates:

$$\mathbb{E}\int_{Y^\pm} |\nabla \tilde{w}^{\pm}_{p,\alpha}|^2 \le C, \quad \mathbb{E}\int_{\Gamma_0} |\tilde{w}^{+}_{p,\alpha} - \tilde{w}^{-}_{p,\alpha}|^2 \le C, \quad \mathbb{E}\int_{Y^\pm} |\tilde{w}^{\pm}_{p,\alpha}|^2 \le \frac{C}{\alpha}. \tag{3.4}$$

Next we argue that for almost all $\gamma \in \mathcal{O}$, the solution $w_{p,\alpha}(\cdot,\gamma)$ above satisfies (3.2) in the usual distributional sense. That is, for any $\varphi(x) \in C^\infty(\mathbb{R}^+_2) \cap C^\infty(\mathbb{R}^-_2)$, whose support is a compact set $K \subset \mathbb{R}^2$, we have

$$\begin{aligned} &\int_{K\cap\Phi(\mathbb{R}^+_2,\gamma)} k_0(p + \nabla w^{+}_{p,\alpha}) \cdot \nabla\overline{\varphi} dx + \int_{K\cap\Phi(\mathbb{R}^-_2,\gamma)} k_0(p + \nabla w^{-}_{p,\alpha}) \cdot \nabla\overline{\varphi} dx \\ &+\alpha\int_K w_{p,\alpha}\overline{\varphi} dx + \int_{K\cap\Phi(\Gamma_2,\gamma)} \frac{1}{\beta}(w^{+}_{p,\alpha} - w^{-}_{p,\alpha} - \beta k_0 p)(\overline{\varphi}^+ - \overline{\varphi}^-) ds(x) = 0. \end{aligned} \tag{3.5}$$

Indeed, due to the regularization, the above problem (with a fixed $\gamma \in \mathcal{O}$) admits a unique solution in the space $H^1_{\mathrm{loc}}(\Phi(\mathbb{R}^+_2,\gamma)) \times H^1_{\mathrm{loc}}(\Phi(\mathbb{R}^-_2,\gamma))$. It can be verified that the solution $w_{p,\alpha}(\cdot,\gamma)$ is stationary and satisfies (3.3); therefore, it must agree with the solution provided by the Lax-Milgram theorem. As a consequence, $w_{p,\alpha}(x,\gamma)$ is also a weak solution in $\mathcal{H}$ to (1.19) in the sense of (3.1).

Applying Corollary A.1.1 and Corollary A.1.2 to the family $\{\tilde{w}_{p,\alpha}\}_\alpha$, we obtain a family $\{\tilde{w}^{\mathrm{ext}}_{p,\alpha} = P\tilde{w}^+_{p,\alpha}\}_\alpha \subset L^2(\mathcal{O}, H^1_{\mathrm{loc}}(\mathbb{R}^2))$ and a family $\{w^{\mathrm{ext}}_{p,\alpha} = P_\gamma w^+_{p,\alpha}\}_\alpha$. Further, $\{\tilde{w}^{\mathrm{ext}}_{p,\alpha}\}_\alpha$ are stationary. They satisfy that $w^{\mathrm{ext}}_{p,\alpha} = \tilde{w}^{\mathrm{ext}}_{p,\alpha} \circ \Phi^{-1}$ and that

$$\mathbb{E}\int_Y |\nabla \tilde{w}^{\mathrm{ext}}_{p,\alpha}|^2 \le C, \quad \mathbb{E}\int_{\Gamma_0} |\tilde{w}^{\mathrm{ext}}_{p,\alpha} - \tilde{w}^-_{p,\alpha}|^2 \le C, \quad \mathbb{E}\int_Y |\tilde{w}^{\mathrm{ext}}_{p,\alpha}|^2 \le \frac{C}{\alpha}. \tag{3.6}$$

Step 2: Extraction of a converging subsequence. The family $\{\tilde{w}^{\mathrm{ext}}_{p,\alpha}\}_\alpha$ may be studied from two view points. Firstly, they form a bounded family in $\widetilde{\mathcal{H}}_S$. Secondly, they belong to $\widetilde{\mathcal{H}}$ and for any compact set $K \subset \mathbb{R}^2$, the estimates (3.6) imply that

$$\mathbb{E}\int_K |\nabla \tilde{w}^{\mathrm{ext}}_{p,\alpha}|^2 \le C(K), \quad \mathbb{E}\int_{\mathbf{\Gamma}\cap K} |\tilde{w}^{\mathrm{ext}}_{p,\alpha} - \tilde{w}^-_{p,\alpha}|^2 \le C(K), \quad \alpha\mathbb{E}\int_K |\tilde{w}^{\mathrm{ext}}_{p,\alpha}|^2 \le C(K). \tag{3.7}$$

From the first point of view, there exists a subsequence, still denoted by $\nabla\tilde{w}^{\mathrm{ext}}_{p,\alpha}$, which converges weakly as $\alpha \downarrow 0$ to a function $\tilde{\eta}^{\mathrm{ext}}_p \in [L^2_S(\mathcal{O}, L^2_{\mathrm{loc}}(\mathbb{R}^2)]^2$ where the subscript S indicates stationary. By a change of variable, we also have that $\nabla w^{\mathrm{ext}}_{p,\alpha}$ converges in $[L^2(\mathcal{O}, L^2_{\mathrm{loc}}(\mathbb{R}^2)]^2$ to η^{ext}_p and

$$\eta^{\mathrm{ext}}_p(y,\gamma) = \nabla_y \Psi(y,\gamma)\tilde{\eta}^{\mathrm{ext}}_p(\tilde{y},\gamma), \tag{3.8}$$

where $\Psi = \Phi^{-1}$ and $\tilde{y} = \Psi(y)$. Moreover, as gradients, $\nabla_{\tilde{y}}\tilde{w}^{\mathrm{ext}}_{p,\alpha}$ and $\nabla_y w^{\mathrm{ext}}_{p,\alpha}$ are curl free. This property is preserved by their limits:

$$\partial_{y_i}(\eta^{\mathrm{ext}}_p)_j = \partial_{y_j}(\eta^{\mathrm{ext}}_p)_i, \quad \partial_{\tilde{y}_i}(\tilde{\eta}^{\mathrm{ext}}_p)_j = \partial_{\tilde{y}_j}(\tilde{\eta}^{\mathrm{ext}}_p)_i, \quad i,j \in \{1,2\}.$$

That is to say, η^{ext}_p and $\tilde{\eta}^{\mathrm{ext}}_p$ are also gradient functions. Consequently, there exist w^{ext}_p and $\tilde{w}^{\mathrm{ext}}_p$ such that $\eta^{\mathrm{ext}}_p = \nabla_y w^{\mathrm{ext}}_p$ and $\tilde{\eta}^{\mathrm{ext}}_p = \nabla_{\tilde{y}}\tilde{w}^{\mathrm{ext}}_p$. The relation (3.8) implies that $w^{\mathrm{ext}}_p(y) = \tilde{w}^{\mathrm{ext}}_p(\Psi(y,\gamma),\gamma) + C_p(\gamma)$ where $C_p(\gamma)$ is a random constant. We hence re-define $\tilde{w}^{\mathrm{ext}}_p$ by adding to it the random variable C_p so that $w^{\mathrm{ext}}_p = \tilde{w}^{\mathrm{ext}}_p \circ \Psi$. By the same token, we have that $\nabla\tilde{w}^-_{p,\alpha}$ and $\nabla w^-_{p,\alpha}$ converge (along the above subsequence) to $\tilde{\eta}^-_p \in [L^2_S(\mathcal{O}, L^2_{\mathrm{loc}}(\mathbb{R}^-_2))]^2$ and $\eta^-_p \in [L^2(\mathcal{O}, L^2_{\mathrm{loc}}(\Phi(\mathbb{R}^-_2)))]^2$ respectively. In addition, for some $\tilde{w}^-_p \in L^2(\mathcal{O}, H^1_{\mathrm{loc}}(\mathbb{R}^-_2))$ and $w^-_p \in L^2(\mathcal{O}, H^1_{\mathrm{loc}}(\mathbb{R}^-_2))$ satisfying that $w^-_p = \tilde{w}^-_p \circ \Psi$, we have $\tilde{\eta}^-_p = \nabla\tilde{w}^-_p$ and $\eta^-_p = \nabla w^-_p$. Similarly, due to the second bound in (3.6), one observes that $\{(\tilde{w}^{\mathrm{ext}}_{p,\alpha} - \tilde{w}^-_{p,\alpha})\big|_{\mathbf{\Gamma}}\}_\alpha$ converges (through a subsequence) to some $\tilde{\zeta}_p \in L^2_S(\mathcal{O}, L^2_{\mathrm{loc}}(\mathbf{\Gamma}))$. Again, by a change of variable, $\{(w^{\mathrm{ext}}_{p,\alpha} - w^-_{p,\alpha})_{\Phi(\mathbf{\Gamma})}\}_\alpha$ converges to certain $\zeta_p \in L^2(\mathcal{O}, L^2_{\mathrm{loc}}(\mathbf{\Gamma}))$ and it holds that $\zeta_p = \tilde{\zeta}_p \circ \Psi$. Finally, since $\tilde{w}^{\mathrm{ext}}_{p,\alpha}$ is stationary, one has $\mathbb{E}\int_Y \nabla_{\tilde{y}}\tilde{w}^{\mathrm{ext}}_{p,\alpha} d\tilde{y} = 0$. Passing to the limit, we get

$$\mathbb{E}\int_Y \nabla_{\tilde{y}}\tilde{w}^{\mathrm{ext}}_p(\tilde{y})d\tilde{y} = 0. \tag{3.9}$$

Now, from the second point of view and the estimate (3.7), we can choose a further subsequence of the converging subsequence obtained from the first view point, still denoted by $\{\tilde{w}_{p,\alpha}\}_\alpha$ and so on, such that the family $\nabla\tilde{w}^{\text{ext}}_{p,\alpha}$ converges in $L^2(\mathcal{O},[L^2_{\text{loc}}(\mathbb{R}^2)]^2)$ to $\tilde{\eta}^{\text{ext}}_p$, $\{\nabla\tilde{w}^-_{p,\alpha}\}_\alpha$ converges to $\tilde{\eta}^-_p$ and $\{(\tilde{w}^{\text{ext}}_{p,\alpha}-\tilde{w}^-_{p,\alpha})|_{\mathbf{\Gamma}}\}_\alpha$ converges in $L^2(\mathcal{O},L^2_{\text{loc}}(\mathbf{\Gamma}))$ to $\tilde{\zeta}_p$. We then verify that these functions are stationary, and by the ergodic theorem they agree with the limits $\tilde{\eta}^{\text{ext}}_p$, $\tilde{\eta}^-_p$ and $\tilde{\zeta}_p$ obtained from the first point of view. As a result, we take expectation on the weak formulation (3.5), and then pass to the limit and obtain (3.1). In other words, the limit $w^{\text{ext}}_p\chi_{\Phi(\mathbb{R}^+_2,\gamma)}+w^-_p\chi_{\Phi(\mathbb{R}^-_2)}\in\mathcal{H}$ provides a weak solution to (1.19) in the sense of (3.1).

Step 3: Uniqueness of the auxiliary problem. It remains to show that the auxiliary equation has unique solution. Suppose otherwise, then there exist v^+_0 and v^-_0 satisfying (3.1) with $p=0$. In addition, there is an extension of $\tilde{v}^+_0$ denoted by $\tilde{v}^{\text{ext}}_0$, such that

$$\nabla\tilde{v}^{\text{ext}}_0 \text{ is stationary,}\quad \text{and}\quad \mathbb{E}\int_Y\nabla\tilde{v}^{\text{ext}}_0dx=0.$$

In the weak formulation of the equations satisfied by (v^+_0,v^-_0), take this function itself as the test function and integrate over $\Phi(NY)$ for a large integer N. We get

$$\mathbb{E}\int_{\Phi(NY\cap\mathbb{R}^+_2)}k_0|\nabla v^+_0|^2dx+\mathbb{E}\int_{\Phi(NY\cap\mathbb{R}^-_2)}k_0|\nabla v^-_0|^2dx \\ +\beta^{-1}\mathbb{E}\int_{\Phi(NY\cap\mathbf{\Gamma})}|v^+_0-v^-_0|^2ds=\mathbb{E}\int_{\partial\Phi(NY)}k_0(n\cdot\nabla v^+_0)\overline{v^+_0}ds.$$

By the elliptic regularity theory adapted to the space $\mathcal{H}$, we know that v^+_0 and v^-_0 are in $L^s(\mathcal{O},W^{1,s}_{\text{loc}}(\Phi(\mathbb{R}^+_2))$ and $L^s(\mathcal{O},W^{1,s}_{\text{loc}}(\mathbb{R}^-_2))$ for some $s>2$. This is is true also for $\tilde{v}^+_0$ and $\tilde{v}^-_0$. To summarize, we have $\nabla\tilde{v}^{\text{ext}}_0$ is stationary, $\mathbb{E}\int_Y\nabla\tilde{v}^{\text{ext}}_0dy=0$ and $\mathbb{E}\|\nabla\tilde{v}^{\text{ext}}_0\|^s_{L^s(Y)}<\infty$ for some $s>2$. These properties of $\tilde{v}^{\text{ext}}_0$ imply that it grows sub-linearly at infinity; see for instance Lemma A.5 of [34]. As a result, v^+_0 also grows sub-linearly at infinity. Consequently, the right-hand side of the previous equality is of order $o(N^2)$. Take the real part of the left-hand side and divided it by N^2, we have

$$\frac{1}{N^2}\sum_{n\in\mathcal{I}(N)}\mathbb{E}\left[\int_{\Phi(Y^+_n)}\sigma_0|\nabla v^+_0|^2dx+\int_{\Phi(Y^-_n)}\sigma_0|\nabla v^-_0|^2dx+\Re\beta^{-1}\int_{\Phi(\Gamma_n)}|v^+_0-v^-_0|^2ds\right]$$

converges to zero as $N\to\infty$ where $\mathcal{I}(N)$ are the indices of cubes $\{Y_n\subset NY\}$. By a change of variable with bounds (1.14) and (1.15), the above implies

$$\frac{1}{N^2}\sum_{n\in\mathcal{I}(N)}\mathbb{E}\left[\int_{Y^+_n}\sigma_0|\nabla\tilde{v}^+_0|^2d\tilde{x}+\int_{Y^-_n}\sigma_0|\nabla\tilde{v}^-_0|^2d\tilde{x}+\beta^{-1}\int_{\Gamma_n}|\tilde{v}^+_0-\tilde{v}^-_0|^2(\tilde{x})ds(\tilde{x})\right]\longrightarrow 0.$$

By the stationarity of the integrands, we rewrite the above equation as

$$\mathbb{E}\int_{Y^+}|\nabla\tilde{v}^+_0|^2d\tilde{x}+\mathbb{E}\int_{Y^-}|\nabla\tilde{v}^-_0|^2d\tilde{x}+\mathbb{E}\int_{\Gamma_0}|\tilde{v}^+_0-\tilde{v}^-_0|^2(\tilde{x})ds(\tilde{x})=0.$$

This implies that $\tilde{v}^+_0=\tilde{v}^-_0=C(\gamma)$ for some random constant. Consequently, $v^+_0=v^-_0=C(\gamma)$ and the uniqueness is proved. □

3.2 Proof of the homogenization theorem

In this section, we prove the homogenization theorem using the energy method, *i.e.*, the method of oscillating test functions [101].

3.2.1 Oscillating test functions

We first build the oscillating test functions. For a fixed vector $p \in \mathbb{R}^2$. Let $(w_p^+, w_p^-) \in \mathcal{H}$ be the unique solution (up to the addition of a random constant) of the auxiliary problem (1.19). In particular, w_p^+ has an extension w_p^{ext}. In the rest of this section, we assume that $\mathbb{E}\int_Y \tilde{w}_p^{\mathrm{ext}} dy = 0$. We define

$$\begin{cases} w_{1p}^{\varepsilon}(x,\gamma) = x \cdot p + \varepsilon w_p^{\mathrm{ext}}(\frac{x}{\varepsilon},\gamma), & x \in \mathbb{R}^2, \\ w_{2p}^{\varepsilon}(x,\gamma) = x \cdot p + \varepsilon Q w_p^-(\frac{x}{\varepsilon},\gamma), & x \in \mathbb{R}^2. \end{cases} \tag{3.10}$$

Here and in the sequel, Q denotes the trivial extension operator which sets $Qf = 0$ outside the spatial support of f. By scaling the auxiliary problem, we verify that $(w_p^{\varepsilon+}, w_p^{\varepsilon-})$, where $w_p^{\varepsilon+}$ is the restriction of w_{1p}^{ε} in $\varepsilon\Phi(\mathbb{R}_2^+)$ and $w_p^{\varepsilon-}$ is the restriction of w_{2p}^{ε} in $\varepsilon\Phi(\mathbb{R}_2^-)$, satisfies

$$\begin{cases} \nabla \cdot k_0 \nabla w_p^{\varepsilon+} = 0 & \text{and} \quad \nabla \cdot k_0 \nabla w_p^{\varepsilon-} = 0 & \text{in } \varepsilon\Phi(\mathbb{R}_2^{\pm}), \\ k_0 n \cdot \nabla w_p^{\varepsilon+} = k_0 n \cdot \nabla w_p^{\varepsilon-} & \text{and} \quad w_p^{\varepsilon+} - w_p^{\varepsilon-} = \varepsilon\beta k_0 n \cdot \nabla w_p^{\varepsilon-} & \text{on } \varepsilon\Phi(\mathbf{\Gamma}). \end{cases}$$

This means that for any test function $\varphi = (\varphi^+, \varphi^-) \in L^2(\mathcal{O}, H^1_{\mathrm{loc}}(\varepsilon\Phi(\mathbb{R}_2^+) \times \varepsilon\Phi(\mathbb{R}_2^-)))$ compactly supported on a bounded open set $\mathscr{O} \subset \mathbb{R}^2$, we have that

$$\begin{aligned} \mathbb{E}\int_{\mathscr{O}\cap\varepsilon\Phi(\mathbb{R}_2^+)} k_0 \nabla w_p^{\varepsilon+} \cdot \overline{\nabla\varphi^+} dx + \mathbb{E}\int_{\mathscr{O}\cap\varepsilon\Phi(\mathbb{R}_2^-)} k_0 \nabla w_p^{\varepsilon-} \cdot \overline{\nabla\varphi^-} dx \\ + (\varepsilon\beta)^{-1}\mathbb{E}\int_{\mathscr{O}\cap\varepsilon\Phi(\mathbf{\Gamma})} (w_p^{\varepsilon-} - w_p^{\varepsilon-})\overline{(\varphi^+ - \varphi^-)} ds = 0. \end{aligned} \tag{3.11}$$

Clearly, this is the scaled version of (3.1). We define also the vector fields $\eta_p^{\varepsilon\pm} = k_0 \nabla w_p^{\varepsilon\pm}$. They satisfy the following convergence results.

Lemma 3.2.1. *Let $w_p^{\varepsilon\pm}$ and the vector fields $\eta_p^{\varepsilon\pm}$ be defined as above and let $\mathscr{O} \subset \mathbb{R}^2$ be a bounded open set. Then as $\varepsilon \to 0$, we have the following:*

$$w_{1p}^{\varepsilon} \to x \cdot p, \qquad \textit{uniformly in } \mathscr{O} \quad \textit{a.s. in } \mathcal{O}; \tag{3.12}$$

$$w_{2p}^{\varepsilon} \to x \cdot p, \qquad \textit{in } L^2(\mathscr{O}) \quad \textit{a.s. in } \mathcal{O}. \tag{3.13}$$

$$Q\eta_p^{\varepsilon\pm} \rightharpoonup \varrho\mathbb{E}\int_{\Phi(Y^{\pm})} k_0 \left(\nabla w_p^{\pm}(x,\cdot) + p\right) dx \qquad \textit{in } [L^2(\mathscr{O})]^2 \quad \textit{a.s. in } \mathcal{O}. \tag{3.14}$$

Proof. To prove the first result, we recall that (w_p^+, w_p^-) solves (3.1) and by the elliptic regularity theorem adapted to the space $\mathcal{H}$ we have

$$\mathbb{E}\int_{\Phi(Y^+,\gamma)} |\nabla w_p^+(x,\gamma)|^s dx < \infty, \quad \text{which implies} \quad \mathbb{E}\int_Y |\nabla \tilde{w}_p^{\mathrm{ext}}(y,\gamma)|^s dy < \infty$$

for some $s > 2$. In addition, $\nabla \tilde{w}_p^{\mathrm{ext}}$ is stationary. By a version of Birkhoff's ergodic theorem, see e.g. Theorem 9 of [80], we have that

$$\lim_{\varepsilon\to 0} \sup_{x\in K} |\varepsilon \tilde{w}^{\mathrm{ext}}(\frac{x}{\varepsilon},\gamma)| = 0 \quad \mathbb{P}\text{-a.s.}$$

for any compact set $K \subset \mathbb{R}^2$. The desired convergence result follows from the relation among w_p^{ext} and $\tilde{w}_p^{\mathrm{ext}}$.

For second convergence result, we first observe the following decomposition

$$w_{2p}^{\varepsilon} - x\cdot p = \varepsilon\left(w_p^-(\frac{x}{\varepsilon}) - w_p^{\mathrm{ext}}(\frac{x}{\varepsilon})\right)\chi_{\varepsilon\Phi(\mathbb{R}_2^-)} + \varepsilon w_p^{\mathrm{ext}}(\frac{x}{\varepsilon})\chi_{\varepsilon\Phi(\mathbb{R}_2^-)}.$$

By the proof of the first result, the second item on the right above converges uniformly in $\mathscr{O}$ to zero and it suffices to show that $J_\varepsilon := \|\varepsilon w_p^-(\varepsilon^{-1}x) - \varepsilon w_p^{\mathrm{ext}}(\varepsilon^{-1}x)\|_{L^2(\varepsilon\Phi(\mathbb{R}_2^-)\cap\mathscr{O})}$ converges to zero. Given $\mathscr{O}$ and ε, we can find $\mathcal{I}_\varepsilon(\mathscr{O}) \subset \mathbb{Z}^2$ such that $\mathscr{O} \subset \cup_{k\in\mathcal{I}_\varepsilon}\varepsilon\Phi(Y_n)$ and $|\mathcal{I}_\varepsilon| \lesssim C(\mathscr{O})\varepsilon^{-2}$. Then a.s. in $\mathcal{O}$ we verify that

$$\begin{aligned} J_\varepsilon &\le \sum_{n\in\mathcal{I}_\varepsilon}\int_{\varepsilon\Phi(Y_n^-)} \varepsilon^2 \left|w_p^{\mathrm{ext}}(\frac{x}{\varepsilon}) - w_p^-(\frac{x}{\varepsilon})\right|^2 dx = \varepsilon^4 \sum_{n\in\mathcal{I}_\varepsilon}\int_{\Phi(Y_n^-)}\left|w_p^{\mathrm{ext}}(x) - w_p^-(x)\right|^2 dx \\ &\le C\varepsilon^4 \sum_{n\in\mathcal{I}_\varepsilon}\int_{Y_n^-}\left|\tilde{w}_p^{\mathrm{ext}}(y) - \tilde{w}_p^-(y)\right|^2 dy. \end{aligned}$$

In the last inequality, we used the change of variable $y = \Phi^{-1}(x)$ and the bounds (1.14) and (1.15). Using the estimate (A.19), we have

$$J_\varepsilon \le C\varepsilon^2\left[\frac{1}{|\mathcal{I}_\varepsilon|}\sum_{n\in\mathcal{I}_\varepsilon}\left(\int_{\Gamma_n}\left|\tilde{w}_p^+(y) - \tilde{w}_p^-(y)\right|^2 ds(y) + \int_{Y_n^-}\left|\nabla\tilde{w}_p^{\mathrm{ext}}(y) - \nabla\tilde{w}_p^-(y)\right|^2 dy\right)\right].$$

Note that the integrands above are stationary and the item inside the bracket is ready for applying ergodic theorem. This item converges to

$$\mathbb{E}\int_{\Gamma_0}|\tilde{w}_p^+ - \tilde{w}_p^-|^2(y)ds(y) + \mathbb{E}\int_Y |\nabla\tilde{w}_p^{\mathrm{ext}} - \nabla\tilde{w}_p^-|^2 dy,$$

which is bounded for example by (3.4) and (3.6). Consequently, $J_\varepsilon \to 0$, proving (3.13).

For the third convergence result, we set first

$$Q\tilde{\eta}_p^{\pm} = (k_0[p + (\nabla\Phi)^{-1}\nabla\tilde{w}_p^{\pm}])\chi_{\mathbb{R}_2^{\pm}}.$$

These functions are stationary and we have the relation $Q\eta_p^{\varepsilon\pm} = (Q\tilde{\eta}_p^{\pm})\left(\Phi^{-1}(\frac{x}{\varepsilon},\gamma)\right)$ holds. By an ergodic theorem adapted to the stationary ergodic setting of this chapter given in Lemma 2.2. of [44], we obtain (3.14). □

3.2.2 Proof of the homogenization theorem

In this subsection we prove the homogenization theorem using Tartar's energy method. Here is the strategy: In the first step, we recall the energy estimates for the solution u_ε to the problem (1.2) and extract a subsequence along which $u_\varepsilon^{\text{ext}}$ converges weakly in $H^1(\Omega)$ to some u_0, and the trivially extended gradient functions $Q\nabla u_\varepsilon^+$ and $Q\nabla u_\varepsilon^-$ has weak limits in $[L^2(\Omega)]^d$. Passing to limits in the weak formulation of (1.2), we obtain equations for these limits and the proper boundary conditions. It worths mentioning that this step can be done for almost all fixed $\gamma \in \mathcal{O}$. In step three we identify u_0 as the unique solution to a homogenized equation. This is done by choosing the oscillating test functions $(\varphi\overline{w_{1p}^\varepsilon}, \varphi\overline{w_{2p}^\varepsilon})$ for the u_ε-equation and the oscillating test functions $(\varphi\overline{u_\varepsilon^+}, \varphi\overline{u_\varepsilon^-})$ for the w_p^ε-equation. After some cancellation one can pass to the limits in these weak formulations of these equations and obtain the weak formulation satisfied by u_0. In this step, we treat the functions as defined in the product space $\mathcal{O} \times \mathbb{R}^2$. The uniqueness of the solution to the weak formulation of u_0 relies on the fact that the trivial extension of u_ε^- converges weakly in $L^2(\Omega)$ to θu_0 for some constant $\theta < 1$. This fact is proved in step two.

Proof of Theorem 1.1.5. Step 1: Extraction of converging subsequences. In this and the next step, the arguments work for any fixed $\gamma \in \mathcal{O}_1$ where $\mathbb{P}(\mathcal{O}) = 1$ and the estimates in (1.13)(1.14)(1.15)(1.16) hold for $\gamma \in \mathcal{O}_1$. We henceforth ignore the dependence on γ. Let $(u_\varepsilon^+, u_\varepsilon^-)$ be the solution to (1.2). In particular, u_ε^+ has an extension $u^{\text{ext}} \in H^1(\Omega)$. Let the vector fields $\xi_\varepsilon^\pm$ be $k_0\nabla u_\varepsilon^\pm$. Then the estimates (1.32) and (1.29) show that

$$\|u_\varepsilon^{\text{ext}}\|_{H^1(\Omega)} + \|Q\xi_\varepsilon^+\|_{[L^2(\Omega)]^2} + \|Q\xi_\varepsilon^-\|_{[L^2(\Omega)]^2} \le C.$$

Consequently, there exists a subsequence and functions $u_0 \in H^1(\Omega)$ and $\xi_1, \xi_2 \in [L^2(\Omega)]^2$, such that

$$\begin{aligned} &u_\varepsilon^{\text{ext}} \rightharpoonup u_0 \text{ weakly in } H^1(\Omega), && u_\varepsilon^{\text{ext}} \to u_0 \text{ strongly in } L^2(\Omega); \\ &Q\xi_\varepsilon^+ \rightharpoonup \xi_1 \text{ weakly in } [L^2(\Omega)]^2, && Q\xi_\varepsilon^- \rightharpoonup \xi_2 \text{ weakly in } [L^2(\Omega)]^2. \end{aligned} \tag{3.15}$$

In the proof of Proposition 1.2.4, we also proved that

$$u_\varepsilon^{\text{ext}}\chi_\varepsilon^- - Qu_\varepsilon^- \to 0 \text{ strongly in } L^2(\Omega). \tag{3.16}$$

Now fix an arbitrary test function $\varphi \in C_0^\infty(\Omega)$. Take $(\varphi\chi_\varepsilon^+, \varphi\chi_\varepsilon^-)$ as a test function in (1.25). Then the interface term disappears and we get

$$\int_\Omega k_0(Q\xi_\varepsilon^+) \cdot \overline{\nabla\varphi} dx + \int_\Omega k_0(Q\xi_\varepsilon^-) \cdot \overline{\nabla\varphi} dx = 0.$$

Passing to the limit $\varepsilon \to 0$ along the subsequence above, one finds

$$\int_\Omega (\xi_1 + \xi_2) \cdot \overline{\nabla\varphi} dx = 0, \quad \forall \varphi \in C_0^\infty(\Omega). \tag{3.17}$$

Therefore, the limiting vector field $\xi_1 + \xi_2$ satisfies that

$$\nabla \cdot (\xi_1 + \xi_2) = 0, \quad \text{in } \mathcal{D}'(\Omega), \tag{3.18}$$

where $\mathcal{D}'(\Omega)$ denotes the space of tempered distributions on Ω. Now for any $\phi \in C^\infty(\partial\Omega)$, we may lift it to a smooth function $\varphi \in C^\infty(\overline{\Omega})$ such that $\varphi = \phi$ on $\partial\Omega$. Take $(\varphi\chi_\varepsilon^+, \varphi\chi_\varepsilon^-)$ as the test function in (1.25) and pass to the limit; we get

$$\int_\Omega (\xi_1 + \xi_2) \cdot \overline{\nabla\varphi} dx = \int_{\partial\Omega} g\overline{\phi}\, ds. \tag{3.19}$$

Since $\xi_1 + \xi_2 \in L^2(\Omega)$ and $\nabla \cdot (\xi_1 + \xi_2) \in L^2(\Omega)$, the trace $n \cdot (\xi_1 + \xi_2)$ on the boundary $\partial\Omega$ is well defined. Applying the divergence theorem and (3.18) we get

$$\int_{\partial\Omega} n \cdot (\xi_1 + \xi_2)\overline{\phi}\, ds = \int_{\partial\Omega} g\overline{\phi}\, ds, \quad \forall \phi \in C^\infty(\overline{\Omega}).$$

This shows that, $n \cdot (\xi_1 + \xi_2) = g$ at $\partial\Omega$. Further, since the trace of $Q\xi_\varepsilon^-$ is zero for all ε, the same argument above shows that $n \cdot \xi_2 = 0$ at $\partial\Omega$. We hence get

$$n \cdot \xi_1 = g \quad \text{at } \partial\Omega.$$

Remark 3.2.1. *It is easy to verify that the weak formulation* (3.17) *works also if we replace the space of test functions by $\varphi \in C_0^\infty(\Omega, L^2(\mathcal{O}))$ and add an integral in γ on the left hand side.*

Step 2: Weak convergence of Qu_ε^-. We can write Qu_ε^- as $u_\varepsilon^{\text{ext}}\chi_\varepsilon^- + (Qu_\varepsilon^- - u_\varepsilon^{\text{ext}}\chi_\varepsilon^-)$. Due to (3.16) and the fact that $u_\varepsilon^{\text{ext}}$ converges strongly to u_0, we only need to verify that χ_ε^- converges weakly to θ. To this purpose, fix an arbitrary open set K compactly supported in Ω, and observe that for sufficiently small ε, K is compactly supported in E_ε defined in (1.18). Then we have

$$\int_K \chi_{\Omega_\varepsilon^-} dx = \int_{K\cap\varepsilon\Phi(\mathbb{R}_2^-)} dx = \int_{\varepsilon\Phi^{-1}\left(\frac{K}{\varepsilon}\right)} \chi_{\mathbb{R}_2^-}(\frac{z}{\varepsilon}) \det \nabla\Phi(\frac{z}{\varepsilon}, \gamma) dz.$$

In [44, 43], it is shown that the characteristic function $\varepsilon\Phi^{-1}\left(\frac{K}{\varepsilon}\right)$ converges strongly in $L^1(\mathbb{R}^2)$ to that of the set $[\mathbb{E}\int_Y \nabla\Phi(y,\cdot)dy]^{-1}K$. On the other hand, since the function $\chi_{\mathbb{R}_2^-}\det\nabla\Phi$ is stationary, by ergodic theorem, we have

$$\chi_{\mathbb{R}_2^-}(\frac{z}{\varepsilon}) \det \nabla\Phi(\frac{z}{\varepsilon}, \gamma) \overset{*}{\rightharpoonup} \mathbb{E}\int_Y \chi_{\mathbb{R}_2^-} \det \nabla\Phi(z, \gamma) dz = \theta\varrho^{-1}, \quad \text{in } L^\infty(\mathbb{R}^2).$$

Here, θ is defined as in (1.20). Consequently, we observe that for any open set K compactly supported in Ω, we have

$$\int \chi_K \chi_{\Omega_\varepsilon^-} dx \to \theta\varrho^{-1} \int_{[\mathbb{E}\int_Y \nabla\Phi(y,\cdot)dy]^{-1}K} dx = \theta\varrho^{-1} \det\left(\mathbb{E}\int_Y \nabla\Phi(y,\cdot)dy\right)^{-1} |K| = \theta|K|.$$

Here, we used the fact that $\det\left(\mathbb{E}\int_Y \nabla\Phi(y,\cdot)dy\right) = \varrho^{-1}$, a fact also proved in [44, 43]. Since linear combinations of characteristic functions of compact sets in Ω are dense in $L^2(\Omega)$, we get the desired result. The fact that $\theta < 1$ is due to the assumption on Y^- and the assumption (1.16). This completes the proof of item two of the theorem up to a subsequence.

Step 3: Identifying the limit. Fix an arbitrary test function $\varphi \in C_0^\infty(\Omega, L^\infty(\mathcal{O}, \mathcal{F}, \mathbb{P}))$. By the constructions of $\Omega_\varepsilon^-, K_\varepsilon$ and E_ε defined in (1.17) and (1.18), for sufficiently small ε, the function φ is compactly supported in E_ε.

Choose $p = e_k, k = 1, 2$ where $e_1 = (1, 0)$ and $e_2 = (0, 1)$. Let $w_{1e_k}^\varepsilon$ and $w_{2e_k}^\varepsilon$ be as in (3.10). In the weak formulation (3.11) of the equations satisfied by them, take $(\overline{\varphi u_\varepsilon^+}, \overline{\varphi u_\varepsilon^-})$ as a test function; we get

$$\mathbb{E}\int_\Omega (Q\eta_{e_k}^{\varepsilon+}) \cdot \nabla(\overline{\varphi} u_\varepsilon^+) dx + \mathbb{E}\int_\Omega (Q\eta_{e_k}^{\varepsilon-}) \cdot \nabla(\overline{\varphi} u_\varepsilon^-) dx \\ + \mathbb{E}\,\frac{1}{\varepsilon\beta}\int_{\Gamma_\varepsilon} (w_{1e_k}^\varepsilon - w_{2e_k}^\varepsilon)\overline{\varphi}(u_\varepsilon^+ - u_\varepsilon^-) ds = 0.$$

Similarly, in the weak formulation (1.25), take $(\varphi\overline{w_{1e_k}^\varepsilon}, \varphi\overline{w_{2e_k}^\varepsilon})$ as the test function; we get

$$\mathbb{E}\int_\Omega (Q\xi_\varepsilon^+) \cdot \nabla(\overline{\varphi} w_{1e_k}^\varepsilon) dx + \mathbb{E}\int_\Omega (Q\xi_\varepsilon^-) \cdot \nabla(\overline{\varphi} w_{2e_k}^\varepsilon) dx \\ + \mathbb{E}\,\frac{1}{\varepsilon\beta}\int_{\Gamma_\varepsilon} (u_\varepsilon^+ - u_\varepsilon^-)\overline{\varphi}(w_{1e_k}^\varepsilon - w_{2e_k}^\varepsilon) ds = 0.$$

Note that the integrating domains in the first formula can be taken as above because φ is compactly supported in E_ε, which implies that $\varepsilon\Phi(\mathbf{\Gamma}) \cap \operatorname{supp}\varphi = \Gamma_\varepsilon \cap \operatorname{supp}\varphi$. Subtracting the two formulas above and noticing in particular that the interface terms cancel out, we get

$$\mathbb{E}\left[\int_\Omega (Q\eta_{e_k}^{\varepsilon+}) \cdot \overline{\nabla\varphi} u_\varepsilon^{\mathrm{ext}} dx + \int_\Omega (Q\eta_{e_k}^{\varepsilon-}) \cdot \overline{\nabla\varphi} u_\varepsilon^{\mathrm{ext}} dx + \int_\Omega (Q\eta_{e_k}^{\varepsilon-}) \cdot \overline{\nabla\varphi}(Qu_\varepsilon^- - u_\varepsilon^{\mathrm{ext}}\chi_\varepsilon^-) dx\right] \\ -\mathbb{E}\left[\int_\Omega (Q\xi_\varepsilon^+) \cdot \overline{\nabla\varphi} w_{1e_k}^\varepsilon dx + \int_\Omega (Q\xi_\varepsilon^-) \cdot \overline{\nabla\varphi} w_{2e_k}^\varepsilon dx\right] = 0.$$

By the convergence results (3.14), (3.12), (3.13), (3.15) and (3.16), we observe that each integrand above is a product of a strong converging term with a weak converging term. Therefore, we can pass the above to the limit $\varepsilon \to 0$ and get

$$\mathbb{E}\int_\Omega (\eta_{1e_k} + \eta_{2e_k}) u_0 \cdot \overline{\nabla\varphi} dx = \mathbb{E}\int_\Omega (\xi_1 + \xi_2) x_k \cdot \overline{\nabla\varphi} dx, \tag{3.20}$$

where η_{1e_k} (resp. η_{2e_k}) is defined as the right-hand side of (3.14) with the "+" (resp. "−") sign. The integral on the right can be written as

$$\mathbb{E}\int_\Omega (\xi_1 + \xi_2) \cdot [\overline{\nabla(\varphi x_k)} - e_k\overline{\varphi}] dx = -\mathbb{E}\int_\Omega (\xi_1 + \xi_2) \cdot e_k\,\overline{\varphi} dx,$$

where we have used (3.17). For the integral involving $\eta_{1e_k} + \eta_{2e_k}$, we check that

$$e_i \cdot (\eta_{1e_k} + \eta_{2e_k}) = k_0\varrho\mathbb{E}\int_{\Phi(Y)} \left(\chi_{\Phi(Y^+)} e_i \cdot \nabla w_{e_k}^+(x, \cdot) + \chi_{\Phi(Y^-)} e_i \cdot \nabla w_{e_k}^-(x, \cdot) + \delta_{ij}\right) dx.$$

This shows that

$$(\eta_{1e_k} + \eta_{2e_k}) u_0 \cdot \overline{\nabla\varphi} = \sum_{j=1}^{2} e_j \cdot (\eta_{1e_k} + \eta_{2e_k}) u_0 \frac{\partial\overline{\varphi}}{\partial x_j} = K_{kj}^* u_0 \frac{\partial\overline{\varphi}}{\partial x_j},$$

where we have used the definition of the matrix (K^*_{ij}) in (1.22). Now (3.20) becomes

$$\mathbb{E}\int_\Omega \sum_{j=1}^{2} K^*_{kj} u_0 \frac{\partial \overline{\varphi}}{\partial x_j} dx = -\mathbb{E}\int_\Omega (\xi_1 + \xi_2)\cdot e_k \,\overline{\varphi} dx.$$

Since $\varphi \in C_0^\infty(\Omega, L^\infty(\mathcal{O}))$ is arbitrary and this functional space is dense in $L^2(\Omega, L^2(\mathcal{O}))$, we conclude that

$$(\xi_1 + \xi_2)\cdot e_k = \sum_{j=1}^{2} K^*_{kj} \frac{\partial u_0}{\partial x_j}, \qquad \text{for all } k,$$

which means precisely that we can substitute this relation in (3.17) and (3.19) with additional integrations in $\mathcal{O}$ and obtain

$$\mathbb{E}\int_\Omega K^*\nabla u_0 \cdot \nabla\overline{\varphi} dx = \mathbb{E}\int_{\partial\Omega} g\overline{\varphi}, \qquad \text{for all } \varphi \in H^1(\Omega, L^2(\mathcal{O})). \tag{3.21}$$

Finally, we recall that for all $\gamma \in \mathcal{O}_1$,

$$\int_\Omega Qu_\varepsilon^+(x,\gamma)dx = 0, \quad \text{and} \quad Qu_\varepsilon^-(\cdot,\gamma) \rightharpoonup \theta u_0(\cdot,\gamma) \text{ weakly in } L^2(\Omega)$$

indicate that

$$\begin{aligned}\int_\Omega u_0(x,\gamma)dx &= \lim_{\varepsilon\to 0}\int_\Omega (Qu_\varepsilon^+(x,\gamma) + Qu_\varepsilon^-(x,\gamma))dx \\ &= \lim_{\varepsilon\to 0}\int_\Omega Qu_\varepsilon^-(x,\gamma)dx = \theta\int_\Omega u_0(x,\gamma)dx.\end{aligned}$$

Since $\theta < 1$, we obtain

$$\int_\Omega u_0(x,\gamma)dx = 0, \qquad \mathbb{P}\text{-a.s.} \tag{3.22}$$

In summary, the weak limit $u_0(x,\gamma)$ provides a solution to the problem (3.21)(3.22). Thanks to this normalization condition, the solution to this problem is unique. Indeed, the difference $v = u_1 - u_2$ of two solutions to this problem would satisfy

$$\mathbb{E}\int_\Omega K^*\nabla v \cdot \nabla\overline{v} dx = 0, \quad \text{and} \int_\Omega v(x,\gamma)dx = 0 \quad \text{holds } \mathbb{P}\text{-a.s.}$$

This can be true only if $v \equiv 0$.

We check that the unique deterministic solution to the homogenized equation (1.21) solves the problem (3.21)(3.22). By uniqueness of the latter problem, we conclude that $u_0(x,\gamma)$ obtained in step one for a.s. $\gamma \in \Omega$ must agree with the deterministic solution to (1.21). We denote this solution as $u_0(x)$. Consequently, all converging subsequences of $(u_\varepsilon^+, u_\varepsilon^-)$ converge to $u_0(x)$ and hence the whole sequence converges to this limit. This completes the proof. □

3.3 Effective admittivity of a dilute suspension

In this subsection, we consider the case when the cells are dilute. We aim to derive a formal first order asymptotic expansion of the effective admittivity in terms of the volume fraction of the dilute cells.

In the formula of the homogenized coefficient (1.22), the integral term has the form

$$J_{ij} = \mathbb{E} \int_{\Phi(Y^+)} e_j \cdot \nabla w^+_{e_i}(y,\cdot)\, dy + \mathbb{E} \int_{\Phi(Y^-)} e_j \cdot \nabla w^-_{e_i}(y,\cdot)\, dy.$$

Thanks to the ergodic theorem, J_{ij} also takes the form

$$J_{ij} = \lim_{N\to\infty} \frac{1}{N^2} \sum_{n\in\mathcal{I}(N)} \left(\int_{\Phi(Y^+_n)} e_j \cdot \nabla w^+_{e_i}(y,\cdot)\, dy + \int_{\Phi(Y^-_n)} e_j \cdot \nabla w^-_{e_i}(y,\cdot)\, dy \right).$$

Here, $\mathcal{I}(N)$ is the indices for the cubes $\{Y_n\}$ inside the big cube NY. Now using integration by parts, we simplify the above expression to

$$J_{ij} = \lim_{N\to\infty} \frac{1}{N^2} \left(\int_{\partial\Phi(NY)} n_j w^+_{e_i}(y,\cdot)\, ds(y) - \sum_{n\in\mathcal{I}(N)} \int_{\Gamma_n} (w^+_{e_i} - w^-_{e_i})(y,\cdot) n_j\, ds(y) \right).$$

Here, n denotes the outer normal vector along the boundary of $\Phi(NY)$ and $\Phi(Y^-_n)$, $n \in \mathcal{I}(N)$; $n_j = n \cdot e_j$ denotes its j-th component. Note that the boundary terms at $\{\partial\Phi(Y_n)\}_{n\in\mathcal{I}(N)} \cap \Phi(NY)$ are cancelled because two adjacent cubes share the same outer normal vector at their common boundary except for reversed signs.

Finally, we have seen that $w^+_{e_i}$ has sub-linear growth. Since the surface $\Phi(NY)$ has volume of order $O(N)$, the sub-linear growth indicates that the boundary integral at $\partial\Phi(NY)$ is of order $o(N^2)$. Consequently, when divided by N^2 this term goes to zero. By applying the ergodic theorem again, we obtain that

$$J_{ij} = \lim_{N\to\infty} \frac{1}{N^2} \sum_{n\in\mathcal{I}(N)} \int_{\Gamma_n} (w^-_{e_i} - w^+_{e_i})(y,\cdot) n_j\, ds(y) = \mathbb{E} \int_{\partial\Phi(Y^-)} (w^-_{e_i} - w^+_{e_i})(y,\cdot) n_j\, ds(y). \tag{3.23}$$

In the following, we investigate this integral further by deriving a formal representation for the jump $w^+_{e_i} - w^-_{e_i}$ in the case when the inclusions are dilute, *i.e.*, small and far away from each other.

To model the dilute suspension, we assume that the reference cell Y^- is of the form of ρB, where B is a domain of unit length scale and unit volume, and $\rho := \sqrt{|Y^-|} \ll 1$ denotes the small length scale of the dilute inclusions. Due to the assumptions (1.14) and (1.15), the length scale of the cell $\Phi(Y^-)$ is still of order ρ. Further, due to the assumption (1.16), the distance of the cell $\Phi(Y^-)$ from the "boundary" $\partial\Phi(Y)$ is of order one, which is much larger than the size of the inclusion.

Since the distances between the inclusions are much larger than their sizes, we may use the single inclusion approximation. That is, $w^{\pm}_{e_i}$ can be approximated by the solutions to the following interface problem:

$$\begin{cases} \nabla \cdot k_0 \nabla w_{e_i}^{\pm} = 0 \text{ in } \Phi(Y^-) \text{ and } \mathbb{R}^2 \setminus \Phi(Y^-), \\ \dfrac{\partial w_{e_i}^+}{\partial n} = \dfrac{\partial w_{e_i}^-}{\partial n}, \text{ and } w_{e_i}^+ - w_{e_i}^- = \rho\beta k_0 (\dfrac{\partial w_{e_i}^-}{\partial n} + n \cdot e_i) \text{ on } \Phi(\Gamma), \\ w_{e_i}^+ \to 0 \text{ at } \infty. \end{cases}$$

Here, $\Phi(\Gamma)$ denotes the boundary of the inclusion. Note that the extra ρ in the jump condition is due to the fact that the length scale of the inclusion $\Phi(Y^-)$ is of order ρ. Using double layer potentials, we represent $w_{e_i}^+$ and $w_{e_i}^-$ as $\mathcal{D}_{\Phi(\Gamma)}[\phi_i]$ restricted to $\Phi(Y^-)$ and $\mathbb{R}^2 \setminus \Phi(Y^-)$ respectively. Due to the trace formula of $\mathcal{D}_{\Phi(\Gamma)}$ and the jump conditions above, the function ϕ_i is determined by

$$-\phi_i = \rho\beta k_0 (\frac{\partial \mathcal{D}_{\Phi(\Gamma)}[\phi_i]}{\partial n} + n_i). \tag{3.24}$$

Let us define the operator $\mathcal{L}_{\Phi(\Gamma)}$ by $\frac{\partial \mathcal{D}_{\Phi(\Gamma)}}{\partial n}$, then we have that

$$w_{e_i}^+ - w_{e_i}^- = -\phi_i = \rho\beta k_0 (I + \rho\beta k_0 \mathcal{L}_{\Phi(\Gamma)})^{-1}[n_i], \quad \text{on } \Phi(\Gamma).$$

As a consequence, we have also that

$$J_{ij} \simeq -\rho\beta k_0 \mathbb{E} \int_{\Phi(\Gamma)} (I + \rho\beta k_0 \mathcal{L}_{\Phi(\Gamma)})^{-1}[n_i] n_j ds.$$

Let us define ψ_i to be $-(I + \rho\beta k_0 \mathcal{L}_{\Phi(\Gamma)})^{-1}[n_i]$, that is $\psi_i + \rho\beta k_0 n \cdot \nabla \mathcal{D}_{\Phi(\Gamma)}[\psi_i](x) = -n_i$. Define the scaled function $\tilde{\psi}_i(\tilde{x}) = \psi_i(\rho\tilde{x})$ on the scaled curve $\rho^{-1}\Phi(\Gamma)$. Using the homogeneity of the gradient of the Newtonian potential, we verify that

$$\mathcal{D}_{\Phi(\Gamma)}[\psi_i](x) = \mathcal{D}_{\rho^{-1}\Phi(\Gamma)}[\tilde{\psi}_i](\tilde{x}), \quad \text{and} \quad \rho n \cdot \nabla \mathcal{D}_{\Phi(\Gamma)}[\psi_i](x) = n \cdot \nabla \mathcal{D}_{\rho^{-1}\Phi(\Gamma)}[\tilde{\psi}_i](\tilde{x}),$$

where $\tilde{x} = \rho^{-1}x$. This shows that $\tilde{\psi}_i = -(I + \beta k_0 \mathcal{L}_{\rho^{-1}\Phi(\Gamma)})^{-1}[n_i]$. Using the change of variable $y \to \rho\tilde{y}$ in the previous integral representation of J_{ij}, we rewrite it as

$$J_{ij} \simeq \rho\beta k_0 \mathbb{E} \int_{\rho^{-1}\Phi(\Gamma)} \psi_i(\rho\tilde{y}) n_j ds(\rho\tilde{y}) = \rho^2 \beta k_0 \mathbb{E} \int_{\rho^{-1}\Phi(\Gamma)} \tilde{\psi}_i n_j ds(\tilde{y}).$$

Finally, the approximation (1.23) of the effective permittivity for the dilute suspension holds, where $f = \varrho\rho^2$ is the volume fraction where ϱ accounts for the averaged change of volume due to the random diffeomorphism; the polarization matrix M is defined by (1.24) and is associated to the deformed inclusion scaled to the unit length scale. Note that the imaging approach developed in subsection 2.11 can be applied here as well.

Chapter 4

Numerical simulations

We present in this section some numerical simulations to illustrate the fact that the Debye relaxation times are characteristics of the microstructure of the tissue.

We use for the different parameters the following realistic values:

- the typical size of eukaryotes cells: $\rho \simeq 10 - 100\ \mu$m;
- the ratio between the membrane thickness and the size of the cell: $\delta/\rho = 0.7 \cdot 10^{-3}$;
- the conductivity of the medium and the cell: $\sigma_0 = 0.5$ S.m^{-1};
- the membrane conductivity: $\sigma_m = 10^{-8}$ S.m^{-1};
- the permittivity of the medium and the cell: $\epsilon_0 = 90 \times 8.85 \cdot 10^{-12}$ F.m^{-1};
- the membrane permittivity: $\varepsilon_m = 3.5 \times 8.85 \cdot 10^{-12}$ F.m^{-1};
- the frequency: $\omega \in [10^4, 10^9]$ Hz.

Note that the assumptions of our model $\delta \ll \rho$ and $\sigma_m \ll \sigma_0$ are verified.

We first want to retrieve the invariant properties of the Debye relaxation times. We consider (Figure 4.1) an elliptic cell (in green) that we translate (to obtain the red one), rotate (to obtain the purple one) and scale (to obtain the dark blue one). We compute the membrane polarization tensor, its imaginary part, and the associated eigenvalues which are plotted as a function of the frequency (Figure 4.2). The frequency is here represented on a logarithmic scale. One can see that for the two eigenvalues the maximum of the curves occurs at the same frequency, and hence that the Debye relaxation times are identical for the four elliptic cells. Note that the red and green curves are even superposed; this comes from the fact that M is invariant by translation.

Next, we are interested in the effect of the shape of the cell on the Debye relaxation times. We consider for this purpose, (Figure 4.3) a circular cell (in green), an elliptic cell (in red) and a very elongated elliptic cell (in blue). We compute similarly as in the preceding case, the polarization tensors associated to the three cells, take their imaginary part and plot the two eigenvalues of these imaginary parts with

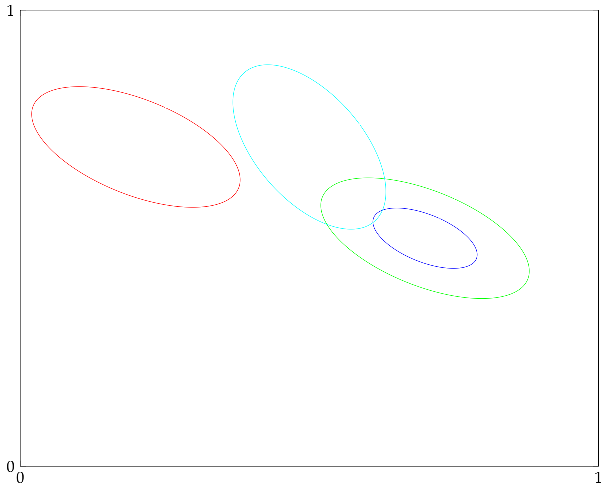

Figure 4.1: *An ellipse translated, rotated and scaled.*

respect to the frequency. As shown in Figure 4.4, the maxima occur at different frequencies for the first and second eigenvalues. Hence, we can distinguish with the Debye relaxation times between these three shapes.

Finally, we study groups of one (in green), two (in blue) and three cells (in red) in the unit period (Figure 4.5) and the corresponding polarization tensors for the homogenized media. The associated relaxation times are different in the three configurations (Figure 4.6) and hence can be used to differentiate tissues with different cell density or organization.

These simulations prove that the Debye relaxation times are characteristics of the shape and organization of the cells. For a given tissue, the idea is to obtain by spectroscopy the frequency dependence spectrum of its effective admittivity. One then has access to the membrane polarization tensor and the spectra of the eigenvalues of its imaginary part. One compares the associated Debye relaxation times to the known ones of healthy and cancerous tissues at different levels. Then one would be able to know using statical tools with which probability the imaged tissue is cancerous and at which level.

In the following examples, we consider the general case of nondilute suspension of cells. We illustrate numerically that the spectral properties of the imaginary part of the effective admittivity tensor are similar to those in the dilute case. In particular, there is a unique maximum with respect to the frequency for the absolute value of each eigenvalue of the imaginary part of the effective admittivity tensor. This maximum is attained again at the inverse of a Debye relaxation time. As for the dilute case, Debye relaxation times are invariant with respect to rigid transformations. Hence, if we consider an elliptic cell, which we tranlate and rotate (Figure 4.7) to obtain three different periodic media, the spectra of their effective admittivity is identical : the red, cyan and green curves are superposed in Figure 4.8. However, they depend in the general case of the volume fraction, the blue curve corresponding to the scaled cell admits its maximum at a different time.Therefore, our classification approach proposed in this part is expected to be applicable for nondilute

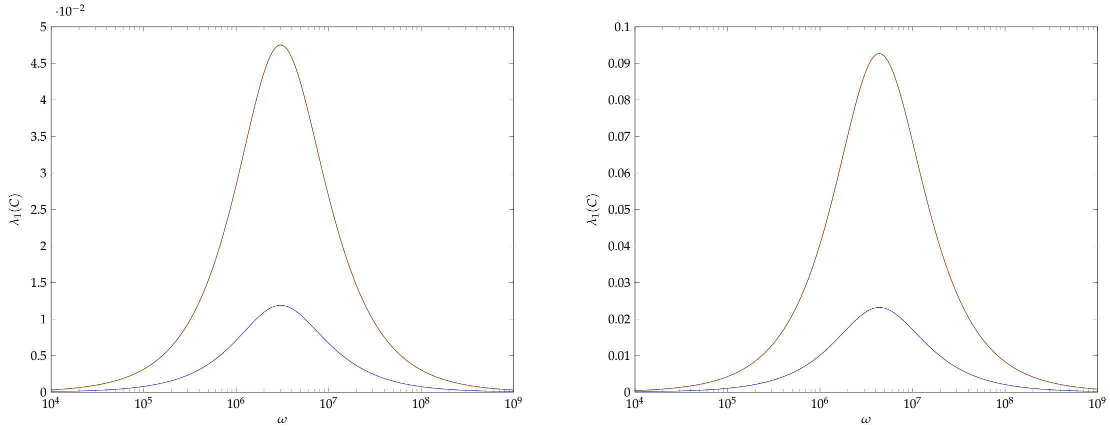

Figure 4.2: *Frequency dependence of the eigenvalues of $\Im M$ for the 4 ellipses in Figure 4.1.*

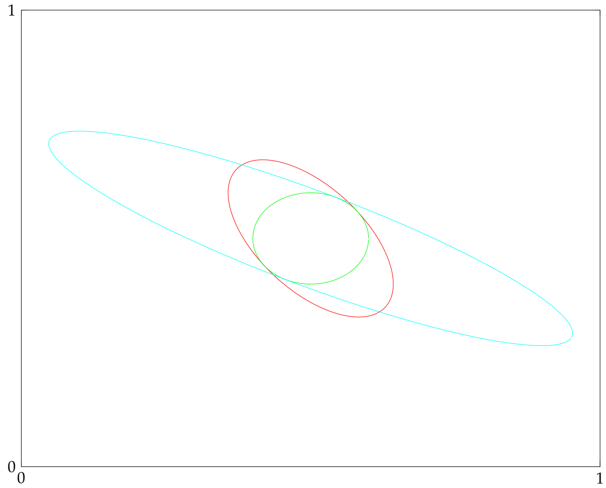

Figure 4.3: *A circle, an ellipse and a very elongated ellipse.*

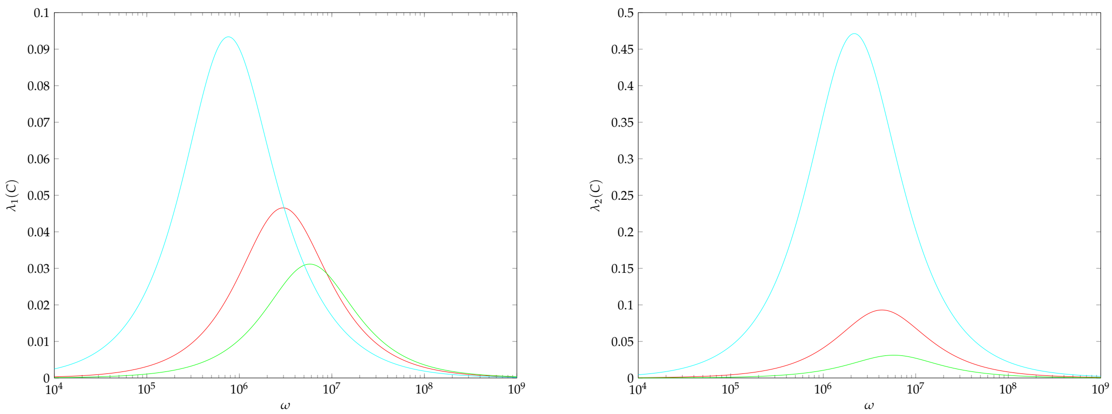

Figure 4.4: *Frequency dependence of the eigenvalues of $\Im M$ for the 3 different cell shapes in Figure 4.3.*

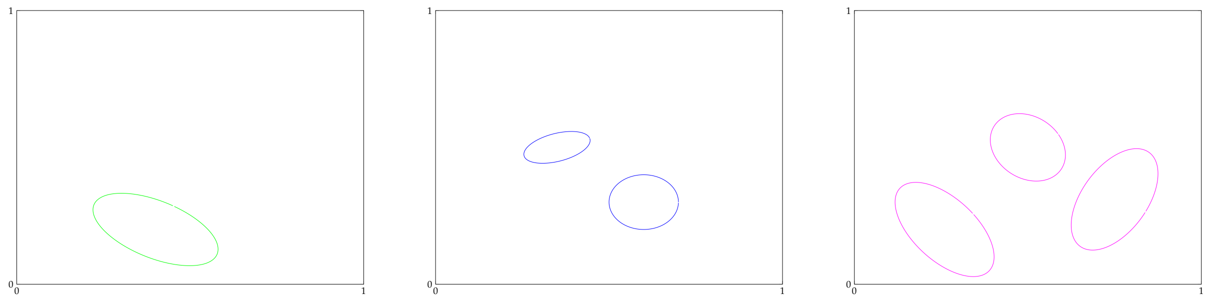

Figure 4.5: *Groups of one, two and three cells.*

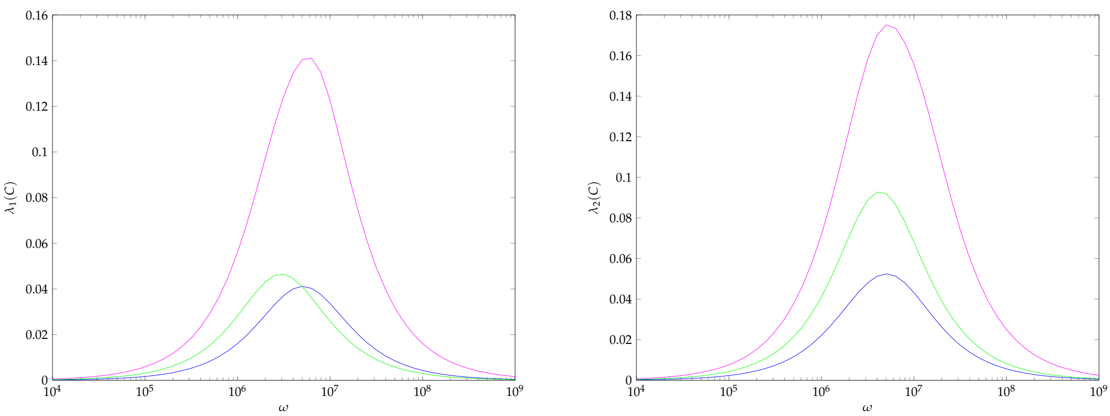

Figure 4.6: *Frequency dependence of the eigenvalues of $\Im M$ in the 3 different cases.*

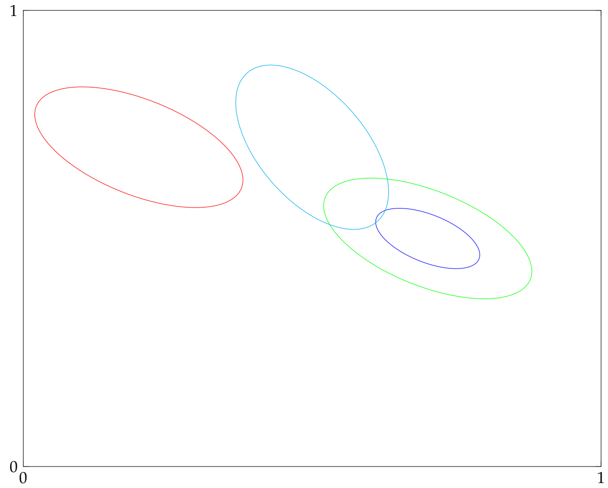

Figure 4.7: *An ellipse translated, rotated and scaled.*

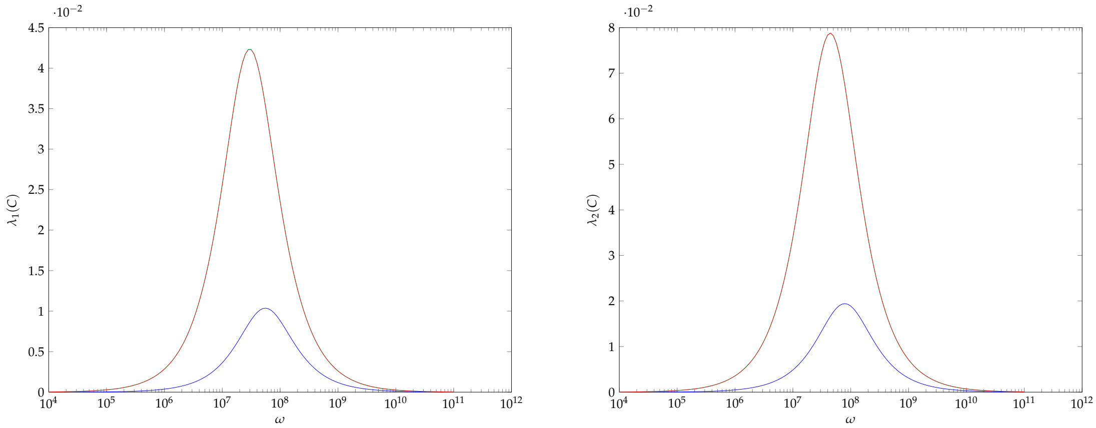

Figure 4.8: *Frequency dependence of the eigenvalues of* $\Im M$ *for the* 4 *ellipses in Figure 4.7.*

suspensions but at given volume fraction. We hence consider three elliptic cells of different shape but with the same volume (Figure 4.9), calculate the imaginary part of their effective admittivity tensor and plot the absolute value of the two associated eigenvalues (Figure 4.10). They attain their maximum for different frequencies. It is worth emphasizing that the numerical results in the general case are obtained using a finite element code with periodic boundary conditions.

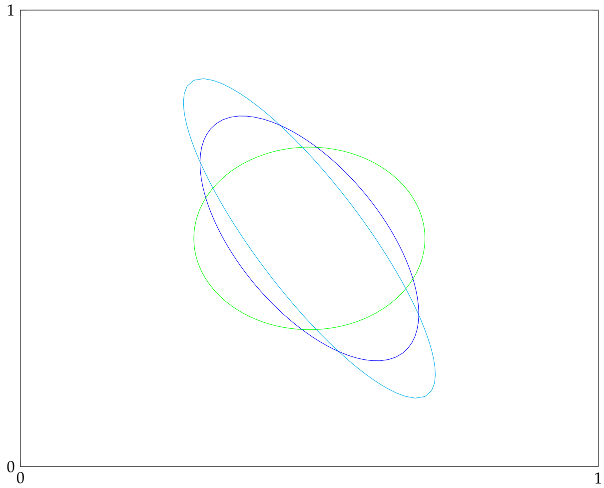

Figure 4.9: *A circle, an ellipse and a very elongated ellipse with same volume.*

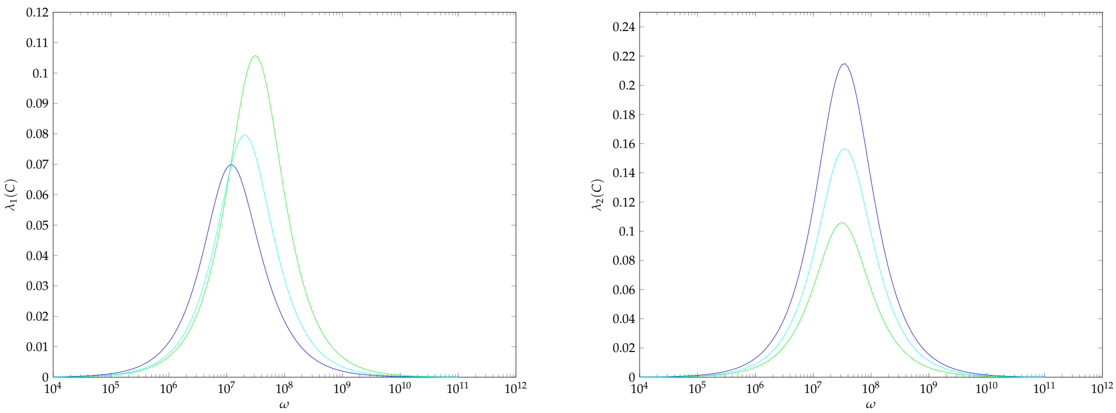

Figure 4.10: *Frequency dependence of the eigenvalues of* $\Im M$ *for the* 3 *different cell shapes in Figure 4.9.*

Part II

Admittivity imaging from multi-frequency micro-electrical impedance tomography

As shown in Part I, spectroscopic admittivity imaging can provide information about the microscopic structure of a medium, from which physiological or pathological conditions of tissue can be derived, because the admittivity of biological tissue varies with its composition, membrane characteristics, intra-and extra-cellular fluids, and other factors.

The aim of Part II is to propose an optimal control optimization algorithm for reconstructing admittivity distributions (i.e., both conductivity and permittivity) from multi-frequency micro-electrical impedance tomography. A convergent and stable optimization scheme is shown to be obtainable from multi-frequency data.

To formulate mathematically the imaging problem, we consider a medium of conductivity σ and permittivity ϵ occupying Ω, $\mathcal{C}^2$-domain of $\mathbb{R}^2$. (Hereafter, the medium is simply called Ω.) The problem of micro–electrical impedance tomography is to reconstruct σ and ϵ from the vector of potential u_ω, $\omega \in (\underline{\omega}, \overline{\omega})$, the solution of

$$\left\{ \begin{array}{rcll} \nabla \cdot (\sigma + i\omega\epsilon)\nabla u_\omega & = & 0 & \text{in } \Omega, \\ u_\omega & = & \varphi & \text{on } \partial\Omega, \end{array} \right. \tag{4.1}$$

where $\varphi = (\varphi_1, \varphi_2) \in H^{1/2}(\partial\Omega)^2$. It is proved in this chapter that the above inverse problem is stably solvable with a good choice of boundary datum φ; that is, φ belongs to what we will refer to as the proper set of boundary measurements; see [14, 123, 129].

Part II is organized as follows. First, in Chapter 5 we review some useful regularity results for elliptic systems of partial differential equations. we also introduce the set of proper boundary measurements. Chapter 6 is devoted to the reconstruction method. We prove that the minimization functional is Fréchet differentiable and we compute its derivative. Then we construct an initial guess and prove the convergence of a minimizing sequence. Chapter 7 is devoted to present numerical illustrations for the convergence and the performance of the proposed optimal control algorithm. In Appendix B, we prove the convergence of Landweber sequences with cutoff functions.

Chapter 5

Regularity results and set of proper boundary conditions

5.1 Preliminaries on regularities

Let $\Omega' = \{x \in \Omega \ : \ \mathrm{dist}(x, \partial\Omega) > c_0\}$ for a small constant $c_0 > 0$. We assume that σ and ϵ are constant and known in $\Omega \setminus \Omega'$. In the following, we let σ_* and ϵ_*, the true conductivity and permittivity of Ω, belong to the convex subset of $H^2(\Omega)^2$ given by

$$\widetilde{\mathcal{S}} = \{(\sigma, \epsilon) := (\sigma_0, \epsilon_0) + (\eta_1, \eta_2) |\, (q_1, q_2) \in \mathcal{S}\},$$

where the positive constants σ_0 and ϵ_0 are respectively the conductivity and permittivity in $\Omega \setminus \Omega'$ and

$$\begin{aligned} \mathcal{S} = \ & \{(\eta_1, \eta_2) \in H_0^2(\Omega)^2 |\ c_1 < \eta_1 + \sigma_0 < c_2,\ c_1 < \eta_2 + \epsilon_0 < c_2,\ \mathrm{supp}\, \eta_j \subset \Omega', \\ & \qquad \|\eta_j\|_{H^2(\Omega)} \leq c_3 \|\eta_j\|_{H^1(\Omega)},\ \|\eta_j\|_{H^1(\Omega)} \leq c_4 \ \text{ for } j = 1, 2 \,\} \end{aligned} \tag{5.1}$$

with c_1, c_2, c_4 and c_4 being positive constants and supp denoting the support. In other words, we can write $\widetilde{\mathcal{S}} = (\sigma_0, \epsilon_0) + \mathcal{S}$. Here, the condition of $\|\eta_j\|_{H^2(\Omega)} \leq c_3 \|\eta_j\|_{H^1(\Omega)}$ is used to exclude any micro-local oscillation on the admittivity distribution.

Introducing an open subset of $\mathbb{C}$

$$\mathcal{O} := \left\{ o \in \mathbb{C} | \Im m\, o < \frac{c_1}{2c_2} \right\}, \tag{5.2}$$

we first establish a useful lemma, which is a direct consequence of standard regularity results.

Lemma 5.1.1. *Let $(\sigma, \epsilon) \in \widetilde{\mathcal{S}}$, $\omega \in \mathcal{O}$, and $f \in L^p(\Omega)$ for $2 \leq p < \infty$. If $v \in H^1(\Omega)$ satisfy*

$$\nabla \cdot (\sigma + i\omega\epsilon) \nabla v = f \quad in \quad \Omega, \tag{5.3}$$

then $v \in W^{2,p}(\Omega')$ and

$$\|v\|_{W^{2,p}(\Omega')} \ \leq \ C \left(\|v\|_{L^p(\Omega)} + \|f\|_{L^p(\Omega)} \right), \tag{5.4}$$

where C depends only on $c_i, i = 0, \dots, 4$, p, and Ω. Moreover, if $v = 0$ on $\partial\Omega$, then

$$\|v\|_{W^{2,p}(\Omega)} \leq C\,(\|v\|_{L^p(\Omega)} + \|f\|_{L^p(\Omega)}). \tag{5.5}$$

Proof. From the standard regularity estimate, we have

$$\|v\|_{H^2(\Omega')} \leq C\,(\|f\|_{L^2(\Omega)^2} + \|v\|_{L^2(\Omega)}). \tag{5.6}$$

The first equation in (5.1.1) can be rewritten as

$$\Delta v = -\nabla v^T \frac{\nabla(\sigma + i\omega\epsilon)}{\sigma + i\omega\epsilon} + \frac{f}{\sigma + i\omega\epsilon}, \tag{5.7}$$

where T denotes the transpose. Since supp $\nabla(\sigma + i\omega\epsilon) \subset \Omega'$, we have

$$\begin{aligned}
\|\nabla v^T \frac{\nabla(\sigma + i\omega\epsilon)}{\sigma + i\omega\epsilon}\|_{L^p(\Omega)} &= \|\nabla v^T \frac{\nabla(\sigma + i\omega\epsilon)}{\sigma + i\omega\epsilon}\|_{L^p(\Omega')} \\
&\leq C\|\nabla v^T\|_{L^{2p}(\Omega')^2} \|\frac{\nabla(\sigma + i\omega\epsilon)}{\sigma + i\omega\epsilon}\|_{L^{2p}(\Omega')^2} \\
&\leq C\|v\|_{H^2(\Omega')} \|\sigma + i\omega\epsilon\|_{H^2(\Omega')} \\
&\leq C\left(\|v\|_{L^2(\Omega')} + \|f\|_{L^2(\Omega)}\right) \|\sigma + i\omega\epsilon\|_{H^2(\Omega')}.
\end{aligned}$$

Here, Schwartz inequality was used for the second inequality; Sobolev embedding for the third inequality; and the last inequality comes from (5.6). Hence, the right side of (5.7) is in $L^p(\Omega)$. Now, we apply the standard $W^{2,p}$-estimate for Poisson's equation (5.7) to get

$$\|v\|_{W^{2,p}(\Omega')} \leq C\left(\|v\|_{L^p(\Omega)^2} + \|f\|_{L^p(\Omega)}\right).$$

□

5.2 Sets of proper boundary conditions

The main purpose of this section is to choose "good" boundary datum φ in (4.1) so that the measurements of the corresponding vector potential u_ω are helpful in our reconstruction algorithm. Such a set of good functions, henceforth coined as *a set of proper boundary conditions*, is defined as follows.

Definition 5.2.1. *Let $\varphi \in H^{1/2}(\partial\Omega)^2$. We say that φ is a proper set of boundary conditions if and only if the 2×2 matrix ∇u_σ is invertible in Ω for all $\sigma \in \sigma_0 + \mathcal{S}$ where the vector u_σ denotes the solution of the boundary value problem*

$$\begin{cases} \nabla \cdot \sigma \nabla u = 0 & \text{in } \Omega, \\ u = \varphi & \text{on } \partial\Omega. \end{cases}$$

The existence of a set of proper boundary conditions was proved in [4, 38, 121]. The following proposition is the main result of this section.

Proposition 5.2.1. *For all $(\sigma, \epsilon) \in \widetilde{\mathcal{S}}$, we denote by u_ω the solution of (4.1) with φ being a proper set of boundary conditions. There exist $N > 1$ open pairwise disjoint open subsets $B_1, B_2, \cdots, B_N$ of Ω, and N frequencies $\omega_1, \cdots, \omega_N \in (\underline{\omega}, \overline{\omega})$ such that*

(i) $\overline{\Omega'} \subset \cup_{j=1}^N \overline{B}_j \subset \Omega$;

(ii) The matrix $A_{\omega_j}(x) = \nabla u_\omega$ is invertible for all $x \in B_j$.

In [3], G. Alberti has proved the result when the dependence of coefficients on the frequency is different from that in our context. The key of his arguments is the fact that u_ω is analytic with respect to ω. Fortunately, his technique is still applicable to (4.1). We present the proof here for the completeness' sake.

Lemma 5.2.1. *Let $\mathcal{O}$ be defined by (5.2). The map*

$$\begin{array}{rccc} L: & \mathcal{O} & \to & H^2_{loc}(\Omega)^2, \\ & \omega & \mapsto & u_\omega, \end{array}$$

where u_ω is the solution to (4.1), is analytic. Moreover, the derivative of L at ω_0 is given by the solution of

$$\left\{ \begin{array}{rcll} \nabla \cdot (\sigma + i\omega_0\epsilon)\nabla w &=& -\nabla \cdot i\epsilon \nabla L(\omega_0) & \textit{in } \Omega, \\ w &=& 0 & \textit{on } \partial\Omega \end{array} \right. \tag{5.8}$$

for all $\omega_0 \in \mathcal{O}$.

Proof. The quotient

$$z := \frac{L(\omega) - L(\omega_0)}{\omega - \omega_0}$$

solves

$$\left\{ \begin{array}{rcll} \nabla \cdot (\sigma + i\omega\epsilon)\nabla z &=& -i\nabla \cdot \epsilon \nabla L(\omega_0) & \text{in } \Omega, \\ z &=& 0 & \text{on } \partial\Omega. \end{array} \right. \tag{5.9}$$

Since $\nabla \cdot \epsilon \nabla L(\omega_0) = 0$ in $\Omega \setminus \overline{\Omega'}$ and $\nabla \cdot \epsilon \nabla L(\omega_0)$ is in $L^2(\Omega')$ (see Lemma 5.1.1), we can use Lemma 5.1.1 again to get

$$\|z\|_{H^2(\Omega)} \leq C\|L(\omega_0)\|_{H^2(\Omega)} \tag{5.10}$$

for some positive constant C.

On the other hand, the difference between z and w satisfies

$$\left\{ \begin{array}{rcll} \nabla \cdot (\sigma + i\omega_0\epsilon)\nabla(z - w) &=& -\nabla \cdot i(\omega - \omega_0)\epsilon\nabla z & \text{in } \Omega, \\ z - w &=& 0 & \text{on } \partial\Omega, \end{array} \right. \tag{5.11}$$

where w is defined by (5.8). Applying Lemma 5.1.1 one more time allows us to obtain

$$\|z - w\|_{H^2(\Omega)} \leq C|\omega - \omega_0|\|\nabla z\|_{H^2(\Omega)}.$$

This, together with (5.10), completes the proof of this lemma. □

We are now in position to prove Proposition 5.2.1.

Proof of Proposition 5.2.1. Let $\Omega'' = \{x \in \Omega : \text{dist}(x, \partial\Omega) > c_0/2\}$, so that $\Omega' \subset\subset \Omega'' \subset\subset \Omega$. From Lemma 5.1.1, $u_\omega \in W^{2,p}(\Omega'')$ for any $p > 2$. Hence, it follows from Sobolev embedding that $u_\omega \in \mathcal{C}^{1,\alpha}(\overline{\Omega''})$ for some $\alpha \in (0,1)$. Thus we can consider u_ω and ∇u_ω pointwisely. We employ the ideas in [3] to prove the proposition. Since $\det : \mathcal{C}(\overline{\Omega''})^{2\times 2} \to \mathcal{C}(\overline{\Omega''})$ is multilinear and bounded and

$$\begin{array}{rcl} \mathcal{O} & \to & \mathcal{C}^{1,\alpha}(\overline{\Omega''})^2 \\ \omega & \mapsto & u_\omega \end{array}$$

is analytic thanks to Lemma 5.2.1. Moreover,

$$\begin{array}{rcl} \mathcal{O} & \to & \mathcal{C}^{0,\alpha}(\overline{\Omega''}) \\ \omega & \mapsto & \det(\nabla u_\omega) \end{array}$$

is also analytic. For $x \in \Omega$, if $\det A_\omega(x) = 0$ for every $\omega \in [\underline{\omega}, \overline{\omega}]$ then for all $\omega \in \mathcal{O}$, $\det A_\omega(x) = 0$ by the analytic continuation theorem. In particular, $\det A_0(x) = 0$ which conflicts with the choice of proper boundary conditions. Hence, we can find $\omega_x \in (\underline{\omega}, \overline{\omega})$ such that $|\det A_{\omega_x}(x)| > 0$. Moreover, since the map $|\det A_{\omega_x}(\cdot)|$ is continuous, it is strictly positive in the ball $B_{r_x}(x)$, centered at x and of radius $r_x > 0$. Noting that $\cup_{x\in\Omega'} B_{r_x}(x)$ covers Ω', we can use the compactness of $\overline{\Omega'}$ in $\mathbb{R}^2$ to complete the proof. $\square$

From now on, a proper set of boundary conditions φ has been chosen. However, in practice, one might not know the values of frequencies and the set $B_1, \cdots, B_N$. We thus suggest to measure the data u_ω for all $\omega \in (\underline{\omega}, \overline{\omega})$. The following corollary of Proposition 5.2.1 will be useful for the sequel.

Corollary 5.2.1. *If φ is a proper set of boundary conditions then we can find $\lambda > 0$ such that*

$$\int_{\underline{\omega}}^{\overline{\omega}} |\det \nabla u_\omega(x)| dx > \lambda,$$

where $u_\omega(x)$ is the solution of (4.1).

Chapter 6

The reconstruction method

6.1 Optimization scheme

Let the function $U_\omega = F[\sigma_*, \epsilon_*; \omega]$ represent the measurement of the solution vector with σ_* and ϵ_* being the true distributions.

Consider

$$\begin{array}{rcl} F: \ \widetilde{\mathcal{S}} \times (\underline{\omega}, \overline{\omega}) & \to & H^2(\Omega)^2 \\ (\sigma, \epsilon; \omega) & \mapsto & u_\omega - U_\omega, \end{array}$$

where again u_ω is the solution to (4.1) with a proper set of boundary conditions φ. Here $\widetilde{\mathcal{S}}$ is considered as a subset of the Hilbert space $H^2(\Omega)^2$. Note that F is well-defined thanks to Lemma 5.1.1.

To reconstruct σ and ϵ, we minimize the discrepancy functional

$$J[\sigma, \epsilon] = \frac{1}{2} \int_{\underline{\omega}}^{\overline{\omega}} \|F[\sigma, \epsilon; \omega]\|^2_{H^1(\Omega)} d\omega$$

for $(\sigma, \epsilon) \in \widetilde{\mathcal{S}}$.

We first investigate the differentiability of F with respect to the pair of admittivity (σ, ϵ). For doing so, we need one more notation. Let $A : B = \sum_{i,j} a_{ij} b_{ij}$ for two matrices $A = (a_{ij})$ and $B = (b_{ij})$. Let $\langle \, , \, \rangle_{H^s}$ denote the $H^s(\Omega)^2$-scalar product for $s = 1, 2$. The following lemma holds.

Lemma 6.1.1. (i) *The map F is Fréchet differentiable in $(\sigma, \epsilon) \in \widetilde{\mathcal{S}}$. For all $(h, k) \in \mathcal{S}$, $DF[\sigma, \epsilon; \omega](h, k)$ is given by the solution of*

$$\left\{ \begin{array}{rcll} \nabla \cdot (\sigma + i\omega\epsilon) \nabla v_\omega & = & -\nabla \cdot (h + i\omega k) \nabla u_\omega & \text{in } \Omega, \\ v_\omega & = & 0 & \text{on } \partial\Omega. \end{array} \right. \tag{6.1}$$

Moreover, DF is Lipschitz continuous with respect to (σ, ϵ).

(ii) *J is Fréchet differentiable in $(\sigma, \epsilon) \in \widetilde{\mathcal{S}}$. Moreover, for all $(h, k) \in \mathcal{S}$,*

$$\begin{aligned} DJ[\sigma, \epsilon](h, k) &= \Re e \int_{\underline{\omega}}^{\overline{\omega}} \langle DF[\sigma, \epsilon; \omega](h, k), F[\sigma, \epsilon; \omega] \rangle_{H^1}, \\ &= \Re e \int_{\underline{\omega}}^{\overline{\omega}} \langle (h, k), DF[\sigma, \epsilon; \omega]^* (F[\sigma, \epsilon; \omega]) \rangle_{H^2}, \end{aligned} \tag{6.2}$$

where $DF[\sigma,\epsilon;\omega]^*$ is the adjoint of $DF[\sigma,\epsilon;\omega]$.

(iii) *Furthermore, for all $(h,k) \in \mathcal{S}$,*

$$DJ[\sigma,\epsilon](h,k) = \Re e \int_{\underline{\omega}}^{\overline{\omega}} \int_\Omega (h+i\omega k)\nabla u_\omega : \nabla p_\omega \, d\omega, \tag{6.3}$$

where $p_\omega \in H^2(\Omega)$ is the solution to the adjoint problem

$$\begin{cases} \nabla\cdot(\sigma+i\omega\epsilon)\nabla p_\omega = \overline{F(\sigma,\epsilon;\omega)} - \Delta\overline{F(\sigma,\epsilon;\omega)} & \text{in } \Omega, \\ p_\omega = 0 & \text{on } \partial\Omega. \end{cases} \tag{6.4}$$

Proof. Take $(h,k)\in\mathcal{S}$ such that $(\sigma+h,\epsilon+k)$ still belongs to $\widetilde{\mathcal{S}}$. Define

$$w_{h,k} = F[\sigma+h,\epsilon+k;\omega] - F[\sigma,\epsilon;\omega] \in H_0^1(\Omega)^2.$$

We have

$$\begin{aligned} \nabla\cdot(\sigma+h+i\omega(\epsilon+k))\nabla w_{h,k} &= -\nabla\cdot(\sigma+h+i\omega(\epsilon+k))\nabla(F[\sigma,\epsilon;\omega]+U_\omega) \\ &= \nabla\cdot(h+i\omega k)\nabla(F[\omega,\sigma,\epsilon]+U_\omega). \end{aligned}$$

Using Sobolev embedding and Lemma 5.1.1, we have

$$\begin{aligned} \|w_{h,k}\|_{H^2(\Omega)^2} &\le C\|\nabla\cdot(h+i\omega k)\nabla(F[\sigma,\epsilon;\omega]+U_\omega)\|_{L^2(\Omega')^2} \\ &\le C\Big(\|h+i\omega k\|_{L^\infty(\Omega')}\|F[\sigma,\epsilon;\omega]+U_\omega\|_{H^2(\Omega')^2} \\ &\qquad +\|\nabla(h+i\omega k)\|_{L^4(\Omega')^2}\|\nabla(F[\sigma,\epsilon;\omega]+U_\omega)\|_{L^4(\Omega')^{2\times 2}}\Big) \\ &\le C\left(\|h\|_{H^2(\Omega)}+\|k\|_{H^2(\Omega)}\right)\left(\|F[\omega,\sigma,\epsilon]\|_{H^2(\Omega')^2}+\|U_\omega\|_{H^2(\Omega')^2}\right). \end{aligned} \tag{6.5}$$

The function $w_{h,k}-v_\omega \in H_0^1(\Omega)$ and satisfies

$$\nabla\cdot(\sigma+i\omega\epsilon)\nabla(w_{h,k}-v_\omega) = -\nabla\cdot(h+i\omega k)\nabla w_{h,k}.$$

Thus, again by repeating the estimates as in (6.5), we get

$$\begin{aligned} \|w_{h,k}-v_\omega\|_{H^2(\Omega)^2} &\le C\left(\|h\|_{H^2(\Omega)}+\|k\|_{H^2(\Omega)}\right)\|w_{h,k}\|_{H^2(\Omega')^2} \\ &\le C\left(\|h\|_{H^2(\Omega)}+\|k\|_{H^2(\Omega)}\right)^2\left(\|F[\omega,\sigma,\epsilon]\|_{H^2(\Omega')^2}+\|U_\omega\|_{H^2(\Omega')^2}\right). \end{aligned}$$

Item (i) has been then proved. Moreover, it is easy to see that DF is Lipschitz continuous with respect to (σ,ϵ). In fact, let (σ,ϵ) and (σ',ϵ') be in $\widetilde{\mathcal{S}}$. Let (h,k) be in $\mathcal{S}$. Then, $DF[\sigma,\epsilon;\omega](h,k) - DF[\sigma',\epsilon';\omega](h,k)$ is solution to the following equation:

$$\begin{cases} \nabla\cdot(\sigma+i\omega\epsilon)\nabla\left(DF[\sigma,\epsilon;\omega](h,k)-DF[\sigma',\epsilon';\omega](h,k)\right) = \\ \qquad -\nabla\cdot(h+i\omega k)\nabla(F[\sigma,\epsilon;\omega]-F[\sigma',\epsilon';\omega]) \\ \qquad -\nabla\cdot(\sigma-\sigma'+i\omega(\epsilon-\epsilon'))\nabla DF[\sigma',\epsilon';\omega](h,k) \quad \text{in}\,\Omega, \\ DF[\sigma,\epsilon;\omega](h,k)-DF[\sigma',\epsilon';\omega](h,k) = 0 \quad \text{on}\,\partial\Omega. \end{cases}$$

Therefore, applying similar estimate as in (6.5), we have

$$\begin{aligned}\|(DF[\sigma,\epsilon;\omega]-DF[\sigma',\epsilon';\omega])(h,k)\|_{H^2(\Omega)^2}\\ \leq C\Big(\|h+i\omega k\|_{H^2(\Omega)}\|F[\sigma,\epsilon;\omega]-F[\sigma',\epsilon';\omega])\|_{H^2(\Omega')^2}\\ +\|\sigma-\sigma'+i\omega(\epsilon-\epsilon')\|_{H^2(\Omega)}\|DF[\sigma',\epsilon';\omega](h,k)\|_{H^2(\Omega)^2}\Big).\end{aligned} \tag{6.6}$$

Since $F[\sigma,\epsilon;\omega]-F[\sigma',\epsilon';\omega]$ satisfies

$$\nabla\cdot(\sigma+i\omega\epsilon)\nabla(F[\sigma,\epsilon;\omega]-F[\sigma',\epsilon';\omega])=-\nabla\cdot(\sigma-\sigma'+i\omega(\epsilon-\epsilon'))\nabla(F[\sigma',\epsilon';\omega]+U_\omega),$$

we apply a similar estimate as in (6.5) to get Lipschitz continuity of F:

$$\begin{aligned}\|F[\sigma,\epsilon;\omega]-F[\sigma',\epsilon';\omega])\|_{H^2(\Omega')} \leq & \; C\|\sigma-\sigma'+i\omega(\epsilon-\epsilon')\|_{H^2(\Omega)}\\ & \times\Big(\|F[\sigma',\epsilon';\omega]\|_{H^2(\Omega')^2}+\|U_\omega\|_{H^2(\Omega')^2}\Big).\end{aligned} \tag{6.7}$$

Noting that $DF[\sigma,\epsilon;\omega](h,k)$ is the solution of (6.1), we also have

$$\|DF[\sigma',\epsilon';\omega](h,k)\|_{H^2(\Omega')}\leq C\|h+i\omega k\|_{H^2(\Omega)}\|\Big(F[\sigma',\epsilon';\omega]\|_{H^2(\Omega')^2}+\|U_\omega\|_{H^2(\Omega')^2}\Big). \tag{6.8}$$

Hence, combining estimates (6.6)-(6.8), we have

$$\begin{aligned}\|DF[\sigma,\epsilon;\omega]-DF[\sigma',\epsilon';\omega]\|_{\mathcal{L}(H^2(\Omega),H^2(\Omega))} \leq & \; C\|\sigma-\sigma'+i\omega(\epsilon-\epsilon')\|_{H^2(\Omega)}\\ & \times\Big(\|F[\sigma',\epsilon';\omega]\|_{H^2(\Omega')^2}+\|U_\omega\|_{H^2(\Omega')^2}\Big).\end{aligned}$$

Item (ii) can be easily proved by using arguments similar to those used above. Item (iii) follows by integration by parts. □

We can now apply the gradient descent method to minimize the discrepancy functional J. We compute the iterates

$$(\sigma_{n+1},\epsilon_{n+1})=T[\sigma_n,\epsilon_n]-\mu DJ[T[\sigma_n,\epsilon_n]], \tag{6.9}$$

where $\mu>0$ is the step size and $T[f]$ is any approximation of the Hilbert projection from $H^2(\Omega)^2$ onto $\overline{\widetilde{\mathcal{S}}}$ with $\overline{\widetilde{\mathcal{S}}}$ being the closure of $\widetilde{\mathcal{S}}$ (in the H^2-norm). The derivative $DJ[T[\sigma_n,\epsilon_n]]$ is given by

$$DJ[T[\sigma_n,\epsilon_n]]=(-\Re e\,\nabla u_\omega:\nabla p_\omega,\omega\Im m\,\nabla u_\omega:\nabla p_\omega),$$

where u_ω and p_ω are respectively the solutions to (4.1) and (6.4) with $(\sigma,\epsilon)=T[\sigma_n,\epsilon_n]$.

The presence of T is necessary because (σ_n,ϵ_n) might not be in $\widetilde{\mathcal{S}}$.

Using (iv) we can show that the optimal control algorithm (6.9) is nothing else than the following Landweber scheme [83, 69] given by

$$\begin{aligned}&(\sigma_{n+1},\epsilon_{n+1})\\ &\quad=T[\sigma_n,\epsilon_n]-\mu\int_{\underline{\omega}}^{\overline{\omega}}DF^*[T[\sigma_n,\epsilon_n];\omega](F[T[\sigma_n,\epsilon_n];\omega])\,d\omega.\end{aligned} \tag{6.10}$$

6.2 Initial guess

To initialize the previous optimal control algorithm, we need to construct an initial guess for the electrical property distributions σ and ϵ.

Consider the solution u_ω to (4.1). For all $x \in \Omega$,

$$\Delta u_\omega + \frac{\nabla u_\omega^T \nabla(\sigma + i\omega\epsilon)}{\sigma + i\omega\epsilon} = 0.$$

It follows that

$$A_\omega^T \frac{\nabla(\sigma + i\omega\epsilon)}{\sigma + i\omega\epsilon} = -\nabla \cdot A_\omega, \tag{6.11}$$

where

$$A_\omega = \nabla u_\omega.$$

Equation (6.11) gives us several ways to reconstruct both σ and ϵ. We suggest to define the map $\gamma_\omega = \log(\sigma + i\omega\epsilon)$, whose imaginary part is chosen in $[0, \frac{\pi}{2})$, and solve

$$\begin{cases} \Delta\gamma_\omega = \nabla \cdot (-(\overline{A_\omega} A_\omega^T)^\dagger \overline{A_\omega} \nabla \cdot A_\omega) & \text{in } \Omega, \\ \gamma_\omega = \log(\sigma_0 + i\omega\epsilon_0) & \text{on } \partial\Omega, \end{cases} \tag{6.12}$$

where † denotes the pseudo-inverse. The knowledge of γ_ω implies those of σ and ϵ. We denote by σ_I and ϵ_I the obtained functions by averaging γ_ω over ω:

$$\sigma_I + i\frac{(\overline{\omega}) + \underline{\omega}}{2}\epsilon_I = \frac{1}{\overline{\omega} - \underline{\omega}} \int_{\underline{\omega}}^{\overline{\omega}} e^{\gamma_\omega} d\omega,$$

where γ_ω is given by (6.12). We use σ_I and ϵ_I as the initial guess for our desired coefficients.

6.3 Convergence of the minimizing sequence

The following theorem holds.

Theorem 6.3.1. *For all $(h, k) \in \mathcal{S}$, we have the following estimate:*

$$\int_{\underline{\omega}}^{\overline{\omega}} \|DF[\sigma, \epsilon; \omega](h, k)\|_{H^1(\Omega)^2} d\omega \geq C\|(h, k)\|_{H^2(\Omega)^2} \tag{6.13}$$

for some positive constant C.

Proof. Assume to the contrary that (6.13) is not true. That means we can find h_n and k_n in $\mathcal{S}$ such that

$$\|h_n\|_{H^2(\Omega)} + \|k_n\|_{H^2(\Omega)} = 1$$

and

$$\int_{\underline{\omega}}^{\overline{\omega}} \|DF[\sigma, \epsilon; \omega](h_n, k_n)\|_{H^1(\Omega)} d\omega \to 0$$

as $n \to \infty$. By compactness, up to extracting a subsequence, we can assume that

$$(h_n, k_n) \rightharpoonup (h, k) \quad \text{in } H_0^1(\Omega)^2. \tag{6.14}$$

Denote by u_ω the vector $F[\sigma, \epsilon; \omega]$ and v_ω^n the vector $DF[\sigma, \epsilon; \omega](h_n, k_n)$. We have

$$v_\omega^n \to 0 \quad \text{in } H_0^1(\Omega)$$

for all $\omega \in (\underline{\omega}, \overline{\omega})$.

Recall $N, B_1, \cdots, B_N, \omega_1, \cdots, \omega_N$, as in Proposition 5.2.1. Fixing $j \in \{1, \cdots, N\}$, we have

$$\begin{aligned} -\nabla \cdot (\sigma + i\omega_j \epsilon) \nabla v_{\omega_j}^n &= \nabla \cdot (h_n + i\omega_j k_n) \nabla u_{\omega_j} \\ &= (\sigma + i\omega_j \epsilon) \nabla u_{\omega_j}^T \nabla \frac{h_n + i\omega_j k_n}{\sigma + i\omega_j \epsilon} \end{aligned}$$

in B_j. Equivalently,

$$\nabla u_{\omega_j}^T \nabla \frac{h_n + i\omega_j k_n}{\sigma + i\omega_j \epsilon} = -\nabla \log(\sigma + i\omega_j \epsilon) \cdot \nabla v_{\omega_j}^n - \Delta v_{\omega_j}^n.$$

Note that the left-hand side of the equation above tends to 0 in $H^{-1}(\Omega)$, so is $\nabla \frac{h_n + i\omega_j k_n}{\sigma + i\omega_j \epsilon}$ in $L^2(B_j)$. By using Poincaré's inequality and the fact that $\overline{\Omega'} \subset \cup_{j=1}^N \overline{B}_j$, we arrive at $h = k = 0$. Since $(h_n, k_n) \in \mathcal{S}$, $\|h_n\|_{H^2(\Omega)} + \|k_n\|_{H^2(\Omega)} \to 0$, which contradicts the assumption. $\square$

Note that as a direct consequence of Theorem 6.3.1, it follows that

$$\left(\int_{\underline{\omega}}^{\overline{\omega}} \|DF[\sigma, \epsilon; \omega](h, k)\|_{H^1(\Omega)^2}^2 d\omega \right)^{\frac{1}{2}} \geq C \|(h, k)\|_{H^2(\Omega)^2} \tag{6.15}$$

for some positive constant C. Hence, Theorem 6.3.1 and Proposition B.0.1 yield our main result in this chapter.

Theorem 6.3.2. *The sequence defined in* (6.10) *converges to the true admittivity* (σ_*, ϵ_*) *of* Ω *in the following sense: there is* $\eta > 0$ *such that if* $\|T[\sigma_I, \epsilon_I] - (\sigma_*, \epsilon_*)\|_{H^2(\Omega)^2} < \eta$, *then*

$$\lim_{n \to +\infty} \|\epsilon_n - \epsilon_*\|_{H^2(\Omega)} + \|\sigma_n - \sigma_*\|_{H^2(\Omega)} = 0.$$

Chapter 7

Numerical illustrations

In this chapter we present some numerical results to illustrate the performance of the proposed optimal control algorithm for admittivity imaging from micro-electrical data.

We consider three regions in the unit square with respective conductivity $2, 3$, and 4. The admittivity of the background medium is $1 + i3\omega$. We produce virtual internal data through the forward problem with the true admittivities. We choose two illuminations $x + ix$, $y + iy$, and calculate the associated potentials u_1 and u_2 in the whole medium with a finite element code. u_1 and u_2 become our measurements for the inverse problem. We first refine the uniform mesh according to the gradient of u_1 and u_2. The initial guess is computed through solving the partial differential equation given in the previous chapter.

We observe that the for the initial guess the permittivities inside the inclusions are different. The reconstruction scheme of the initial guess couples the distributions of the conductivities with those of the permittivities.

It is worth emphasizing that in our case the matrix data is invertible everywhere in the domain and therefore, there is no need for taking multi-frequency measurements.

The results of the reconstructions are presented after 20 and 40 iterations. The difference between the true and reconstructed conductivities are shown. After 20 iterations, the shapes of the inclusions are well reconstructed however the values of the conductivity inside are still not correct. 40 iterations are enough to well reconstruct both the shapes, the conductivities, and the permittivities.

In the second set of numerical examples, we consider a different phantom. The conductivities are between 1 and 2 as shown below while the permittivity is constant and equal to 3 everywhere. Again, after 40 iterations starting from the initial guess computed by solving the PDE problem, the reconstructed images are well resolved.

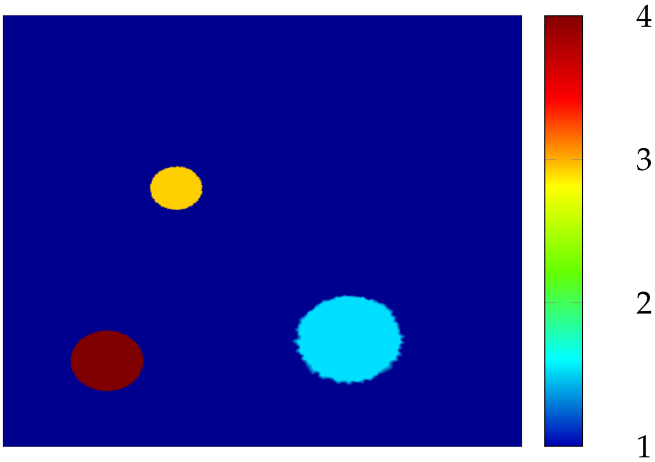

Figure 7.1: *True conductivity* σ_*.

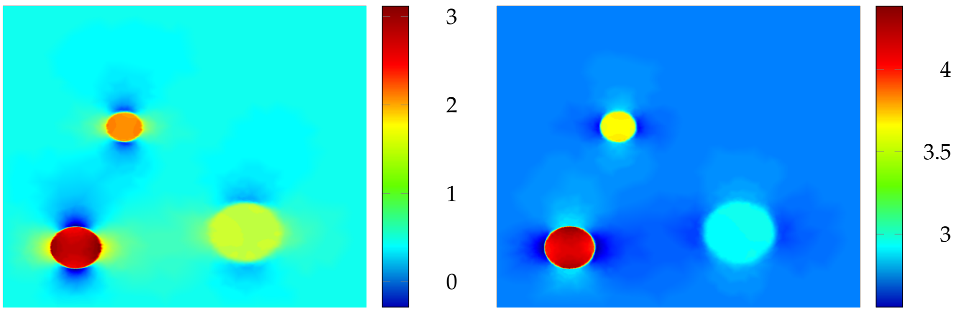

Figure 7.2: *Initial guess of the conductivity (on the left) and the permittivity (on the right).*

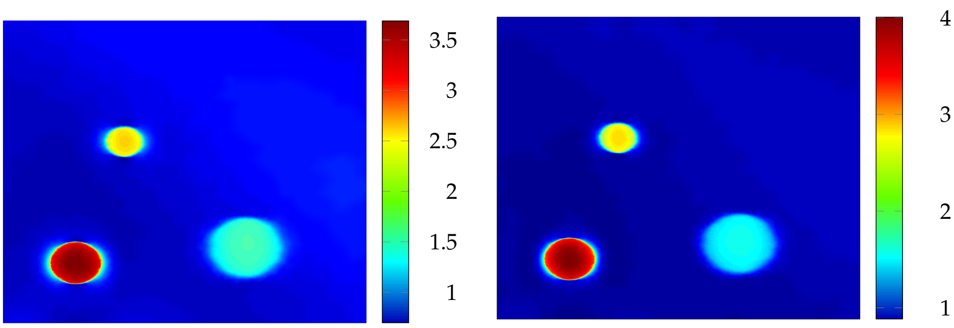

Figure 7.3: *Reconstructed conductivity after* 20 *(on the left) and* 40 *(on the right) iterations of the algorithm.*

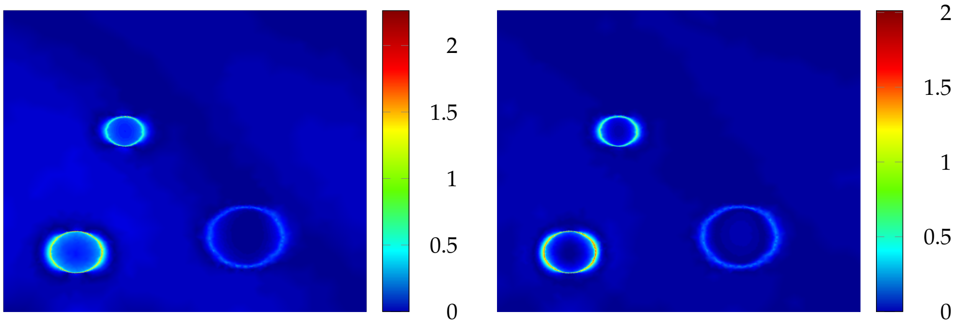

Figure 7.4: *Absolute value of the difference between the reconstructed and true conductivities after* 20 *(on the left) and* 40 *(on the right) iterations.*

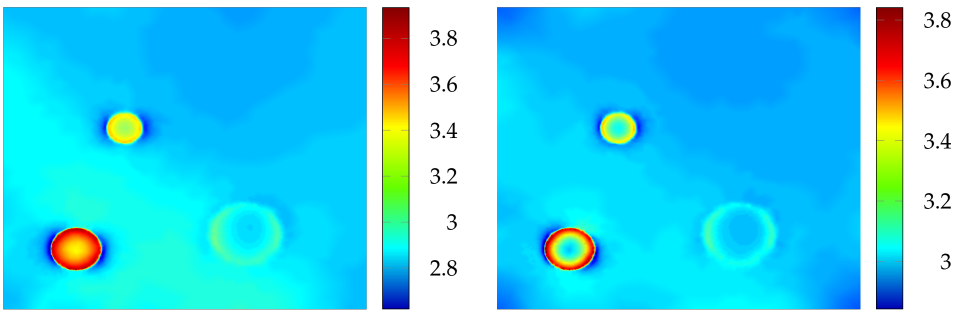

Figure 7.5: *Reconstructed permittivity after* 20 *(on the left) and* 40 *(on the right) iterations of the algorithm.*

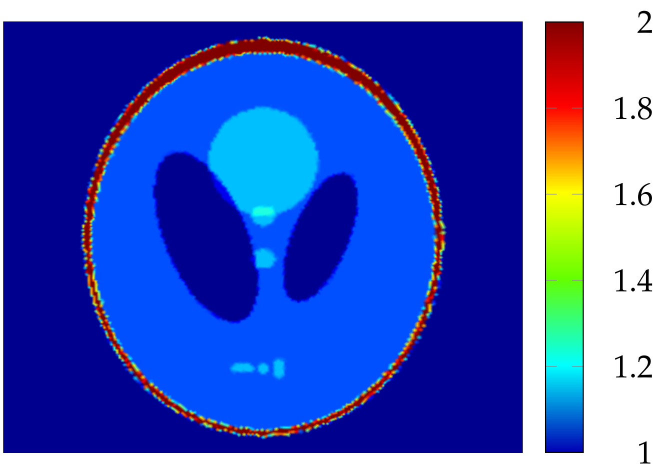

Figure 7.6: *True conductivity* σ_*.

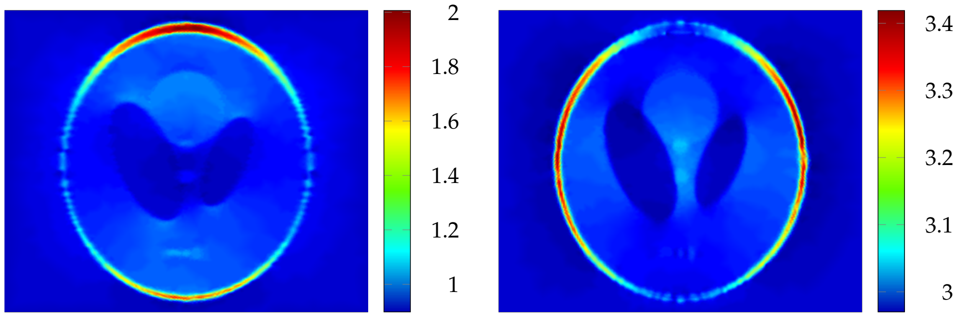

Figure 7.7: *Initial guess of the conductivity (on the left) and the permittivity (on the right).*

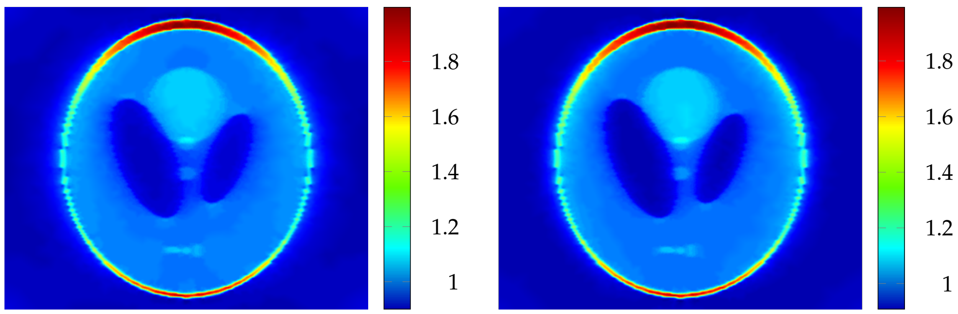

Figure 7.8: *Reconstructed conductivity after* 20 *(on the left) and* 40 *(on the right) iterations of the algorithm.*

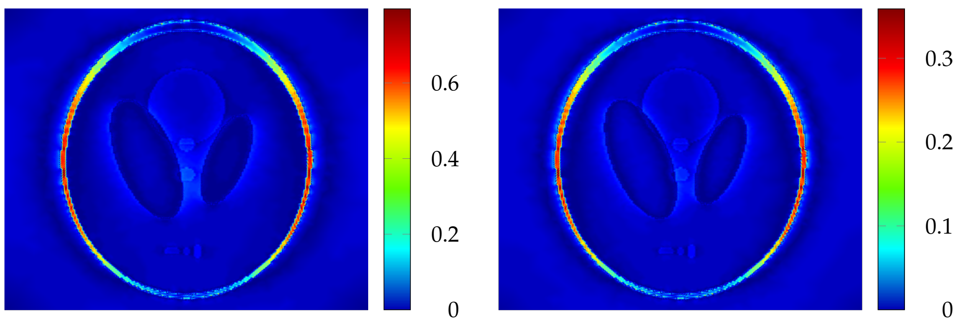

Figure 7.9: *Absolute value of the difference between the reconstructed and true conductivities after* 20 *(on the left) and* 40 *(on the right) iterations.*

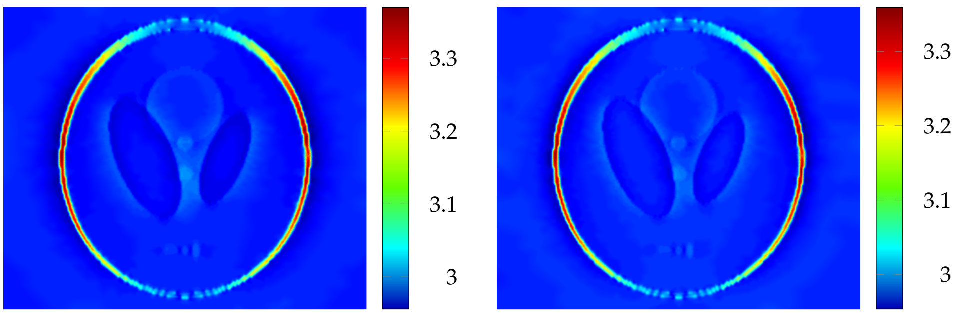

Figure 7.10: *Reconstructed permittivity after* 20 *(on the left) and* 40 *(on the right) iterations of the algorithm.*

Part III

Mathematical modeling of fluorescence diffuse optical imaging of cell membrane potential changes

The purpose of Part III is threefold. We first provide and analyze a mathematical model for optical imaging of changes in membrane electric potentials. Then we propose, in the linearized case where the shape of the cell is a perturbation of a disk, an efficient direct imaging technique based on an appropriate choice of the applied currents. An iterative imaging algorithm for more complex shapes is also suggested. Finally, we estimate the resolving power of the proposed imaging algorithm in the presence of measurement noise.

Our main results in Part III can be formulated as follows. Let C be the cell, and let Ω be the background domain. Given an optical excitation g, the emitted light fluence is Φ^g_{emt}, the solution to the diffusion equation (8.3) with Φ^g_{exc} defined by (8.2) and c_{flr} being the concentration of fluorophore supported on the cell membrane ∂C. Equation (8.5) gives the relation between the function c_{flr} and the electric potential u defined by (8.4). In order to image the cell membrane ∂C, we establish identity (10.1) and linearize in Theorem 10.2.1 relation (8.5) for ∂C being a perturbation of a disk. Proposition 10.2.7 gives the least squares estimate of the cell membrane perturbation. Introducing the signal-to-noise ratio in (10.55), where σ models the measurement noise amplitude and ϵ corresponds to the order of magnitude of the cell membrane perturbation, we derive in Theorem 10.2.2 the resolving power of the imaging method. Theorem 10.2.3, which is our main result in this chapter, provides expressions for the reconstructed modes in the cell membrane perturbation in the presence of measurement noise under physical assumptions on the size of the cell and the value of the used frequency. A generalization of the linearization procedure for arbitrary shaped cell membranes is provided in Proposition 10.3.1, and the reconstruction of perturbations of arbitrary-shaped cell membranes is formulated as a minimization problem, where the data is appropriately chosen in order to maximize the resolution of the reconstructed images.

Part III is organized as follows. Chapter 8 is devoted for the governing model of the hybrid membrane imaging technique. In Chapter 9 the forward problems are analyzed. Chapter 10 presents the membrane reconstruction technique. Numerical results to illustrate the viability and the limitations of the proposed membrane reconstruction technique are given.

Chapter 8

Governing model for the hybrid membrane imaging technique

We consider a cell that we want to image. We inject fluorescent indicators that stick only on the cell membrane [97]. These markers are chosen so that their concentration responds linearly to the potential jump across the membrane, when the cell is immersed in an external electric field [68]. We apply such an external electric field at the boundary of our domain and use fluorescence optical diffuse tomography to reconstruct the position and shape of the membrane.

8.1 Coupled diffusion equations

A sinusoidally modulated near infrared monochromatic light source g, located at the boundary $\partial\Omega$ of the examined domain Ω, launches an excitation light fluence

$$\phi_{\text{exc}} = \Phi_{\text{exc}}(x, \omega)\, e^{i\omega t}$$

at the wavelength λ_{exc}, into Ω. At time t and point x, ϕ_{exc} represents the average photon density, due to excitation by the source oscillating at frequency ω. After it undergoes multiple scattering and absorption, this light wave reaches the fluorescent markers that are accumulated on ∂C, the membrane of the cell C. The excited fluorophores emit a wave

$$\phi_{\text{emt}} = \Phi_{\text{emt}}(x, \omega)\, e^{i\omega t}$$

at the wavelength λ_{emt}. The intensity of the emitted wave is proportional to the intensity of the excitation wave when it reaches the fluorescent molecule. The emitted waves pass through the absorbing and scattering domains and are detected at the boundary $\partial\Omega$.

In the near infrared spectral window, the propagation of light in biological tissues can be modeled by the diffusion equation, which is a limit of the radiative transport equation when the transport mean free path is much smaller than the typical propagation distance. Our model can therefore be described by the following coupled diffusion equations completed by Robin boundary conditions [125, 107, 72, 117]:

$$\begin{cases} -\nabla \cdot (D_{\text{exc}}(x)\nabla\Phi_{\text{exc}}(x,\omega)) + \left(\mu_{\text{exc}}(x) + \dfrac{i\omega}{c}\right)\Phi_{\text{exc}}(x,\omega) = 0 & \text{in}\,\Omega, \\ \ell_{\text{exc}}\dfrac{\partial\Phi_{\text{exc}}}{\partial\nu}(x,\omega) + \Phi_{\text{exc}}(x,\omega) = g(x) & \text{on}\,\partial\Omega, \end{cases}$$

$$\begin{cases} -\nabla \cdot (D_{\text{emt}}(x)\nabla\Phi_{\text{emt}}(x,\omega)) + \left(\mu_{\text{emt}}(x) + \dfrac{i\omega}{c}\right)\Phi_{\text{emt}}(x,\omega) \\ \qquad = \gamma(x,\omega)\,\Phi_{\text{exc}}(x,\omega) \quad \text{in}\,\Omega, \\ \ell_{\text{emt}}\dfrac{\partial\Phi_{\text{emt}}}{\partial\nu}(x,\omega) + \Phi_{\text{emt}}(x,\omega) = 0 \quad \text{on}\,\partial\Omega. \end{cases}$$

Here,

- ν denotes the outward normal at the boundary $\partial\Omega$;
- c denotes the speed of light in the medium;
- D_{exc} and μ_{exc} (respectively D_{emt} and μ_{emt}) denote the photon diffusion and absorption coefficient at wavelength λ_{exc} (respectively λ_{emt}) over the speed of light c. Assuming that the scattering is isotropic, they can be expressed, for $i = \text{exc}, \text{emt}$, as follows:

  $$D_i(x) = \frac{1}{d(\mu_{a,i}(x) + \mu_{\text{flr},i}(x) + \mu'_{s,i}(x))} \quad \text{and} \quad \mu_i(x) = \mu_{a,i}(x) + \mu_{\text{flr},i}(x)\,,$$

  where

  - $\mu_{a,i}$ denotes the absorption coefficient, due to natural chromophores of the medium, at wavelength λ_i;
  - $\mu_{\text{flr},i}$ denotes the absorption coefficient, due to fluorophores, at wavelength λ_i. This absorption coefficient is proportional to the fluorophore concentration $c_{\text{flr}}(x)$. The proportionality coefficient, ε_{exc}, is the fluorophore extinction coefficient at wavelength λ_i;
  - $\mu'_{s,i}$ denotes the reduced scattering coefficient at wavelength λ_i; its inverse is the transport mean free path.
  - ℓ_i is the extrapolation length. It is computed from the radiative transport theory [116] and is proportional to the transport mean path. The multiplicative function depends on the index mismatch between the scattering medium in Ω and the surroundings.
  - d is the space dimension;

- γ is given by

  $$\gamma(x,\omega) = \frac{\eta\,\mu_{\text{flr,exc}}(x)}{1 - i\omega\tau(x)} = \frac{\eta\varepsilon_{\text{exc}}\,c_{\text{flr}}(x)}{1 - i\omega\tau(x)}, \tag{8.1}$$

  with η and τ being respectively the fluorophore's quantum efficiency and fluorescence lifetime.

8.2 Model assumptions

Let Ω be the background domain and let $C \Subset \Omega$ denote the cell. From now on, the space dimension d is equal to 2 or 3 and Ω and C are bounded $\mathcal{C}^2$- domains.

The fluorophores are only located on the cell membrane ∂C; their concentration $c_{\text{flr}}(x)$ is zero, except on ∂C. We neglect their contribution to the absorption and diffusion coefficient, that is,

$$D_i(x) = \frac{1}{d(\mu_{a,i}(x) + \mu'_{s,i}(x))} \quad \text{and} \quad \mu_i(x) = \mu_{a,i}(x).$$

In the near infrared spectral window, the absorption coefficient is much smaller than the reduced scattering coefficient. This is one of the conditions to approximate the light propagation in the medium by the diffusion equation.

We can approximate the diffusion coefficients at the excitation and emission wavelength as follows:

$$D_i(x) = \frac{1}{d\mu'_{s,i}(x)}.$$

We consider that the optical parameters are constant in the domain Ω and do not depend on the wavelength of the propagating light. Hence, for $i = \text{exc}, \text{emt}$,

$$D_i(x) = D_i = D = \frac{1}{d\mu'_s}, \quad \mu_i(x) = \mu_i = \mu = \mu_a, \quad \text{and} \quad \ell_i(x) = \ell_i = \ell.$$

We consider that the fluorophore's fluorescence lifetime τ is constant. From (8.1) it follows that γ depends on the position x only through $\mu_{\text{flr}}(x)$ and, more specifically, $c_{\text{flr}}(x)$. It can then be written as follows:

$$\gamma(x,\omega) = \tilde{\gamma}(\omega)\, c_{\text{flr}}(x) \quad \text{with} \quad \tilde{\gamma}(\omega) = \frac{\eta\varepsilon_{\text{exc}}}{1 - i\omega\tau}.$$

The coupled diffusion equations and their boundary conditions then become

$$\begin{cases} -D\Delta\Phi^g_{\text{exc}}(x,\omega) + \left(\mu + \dfrac{i\omega}{c}\right)\Phi^g_{\text{exc}}(x,\omega) = 0 & \text{in}\,\Omega, \\ \ell\dfrac{\partial\Phi^g_{\text{exc}}}{\partial\nu}(x,\omega) + \Phi^g_{\text{exc}}(x,\omega) = g(x) & \text{on}\,\partial\Omega, \end{cases} \tag{8.2}$$

$$\begin{cases} -D\Delta\Phi^g_{\text{emt}}(x,\omega) + \left(\mu + \dfrac{i\omega}{c}\right)\Phi^g_{\text{emt}}(x,\omega) = \tilde{\gamma}(\omega)\, c_{\text{flr}}(x)\, \Phi^g_{\text{exc}}(x,\omega) & \text{in}\,\Omega, \\ \ell\dfrac{\partial\Phi^g_{\text{emt}}}{\partial\nu}(x,\omega) + \Phi^g_{\text{emt}}(x,\omega) = 0 & \text{on}\,\partial\Omega, \end{cases} \tag{8.3}$$

where the source g is in $L^2(\partial\Omega)$.

8.3 Electrical model of a cell

Here we use the same electrical model of a cell as in Section 1.1.2 but under a direct courant.

We apply at the boundary of our domain an electric field $g_{\text{ele}} \in L^2(\partial\Omega)$. We consider that $\Omega \setminus \overline{C}$ and C are homogeneous and isotropic media with conductivity 1. The thickness ϵ of the cell membrane is supposed to be small. We denote by σ the conductivity of the cell membrane. We assume that $\sigma \ll 1$ and $\beta > 0$ to be given by $\beta = \sigma^{-1}\epsilon$; see [90].

We can approximate the voltage potential u within our medium by the unique solution to the following problem [52, 108, 77, 109, 110]:

$$\begin{cases} \Delta u = 0 & \text{in } C \cup \Omega \setminus \overline{C}, \\ \left.\dfrac{\partial u}{\partial \nu}\right|_{+} - \left.\dfrac{\partial u}{\partial \nu}\right|_{-} = 0 & \text{on } \partial C, \\ u\,|_{+} - u\,|_{-} = \beta \dfrac{\partial u}{\partial \nu} & \text{on } \partial C, \\ \left.\dfrac{\partial u}{\partial \nu}\right|_{\partial\Omega} = g_{\text{ele}}, & \displaystyle\int_{\partial\Omega} u = 0. \end{cases} \tag{8.4}$$

Since we have chosen the fluorescent indicators of the cell membrane such that they respond linearly to the potential jump across the membrane [68], we can express their concentration as

$$c_{\text{flr}} = \delta\,[u]\big|_{\partial C}, \tag{8.5}$$

where δ is a constant [68].

Chapter 9

Analysis of the forward problem

The forward problem consists of determining $\Phi_{\text{emt}}|_{\partial\Omega}$, for a fixed applied electric field g_{ele}, a light excitation g and a given cell C. The optical parameters of the medium, D and μ, the speed of light c, the extrapolation length ℓ and $\tilde{\gamma}$ are supposed to be known.

9.1 Expression of Φ_{exc}^{g}

Let Φ_{exc}^{g} be the excitation light fluence in Ω, due to an excitation g applied at its boundary $\partial\Omega$. The function Φ_{exc}^{g} is the solution to the following problem:

$$\begin{cases} -\Delta\Phi_{\text{exc}}^{g}(y) + k^2\,\Phi_{\text{exc}}^{g}(y) = 0 & \text{in}\,\Omega, \\ \ell\dfrac{\partial\Phi_{\text{exc}}^{g}}{\partial\nu}(y) + \Phi_{\text{exc}}^{g}(y) = g & \text{on}\,\partial\Omega, \end{cases} \tag{9.1}$$

where $k^2 = \dfrac{\mu + i\omega/c}{D}$. Note that if $\ell = 0$, then the Robin boundary condition in (9.1) should be replaced with the Dirichlet boundary condition: $\Phi_{\text{exc}}^{g}(y) = g$ on $\partial\Omega$. The following result holds.

Theorem 9.1.1. *There exists a unique solution Φ_{exc} in $H^1(\Omega)$ to (9.1).*

Proof. The variational formulation of (9.1) is given by

$$\text{Find}\ \Phi_{\text{exc}} \in H^1(\Omega)\ \text{such that for all}\ \Psi \in H^1(\Omega):$$
$$\begin{cases} \displaystyle\int_{\Omega} \nabla\Phi_{\text{exc}}(x)\cdot\nabla\overline{\Psi}(x)\,dx + k^2\int_{\Omega}\Phi_{\text{exc}}\overline{\Psi}(x)\,dx \\ \displaystyle\qquad\qquad + \frac{1}{\ell}\int_{\partial\Omega}\Phi_{\text{exc}}\overline{\Psi}\,d\sigma(x) = \frac{1}{\ell}\int_{\partial\Omega} g\overline{\Psi}\,d\sigma(x). \end{cases}$$

Since $\mathcal{R}e(k^2) = \dfrac{\mu}{D} > 0$, we can apply Lax-Milgram theorem and prove existence and uniqueness in $H^1(\Omega)$ of a solution for (9.1). □

Let Γ be the fundamental solution to $-\Delta + k^2$. Γ is (the exponentially decaying) solution to

$$\forall\, y, z \in \mathbb{R}^d, \quad -\Delta_y \Gamma_z(y) + k^2\, \Gamma_z(y) = \delta_z(y), \tag{9.2}$$

where δ_z is the Dirac mass at z.

We know the explicit expression of $\Gamma_z(y)$ for all $y \neq z \in \mathbb{R}^d$ [29]:

$$\Gamma_z(y) = \frac{i}{4}\, H_0^{(1)}(ik|y-z|) \qquad \text{if}\, d = 2,$$

$$\Gamma_z(y) = \frac{e^{-k|y-z|}}{4\pi|y-z|} \qquad \text{if}\, d = 3,$$

where $H_0^{(1)}$ is the Hankel function of the first kind of order 0.

We introduce the single and double layer potentials of a function $f \in L^2(\partial\Omega)$, for all $z \in \mathbb{R}^d \setminus \partial\Omega$, [29]:

$$\forall\, z \in \mathbb{R}^d, \quad \mathcal{S}_\Omega[f](z) = \int_{\partial\Omega} \Gamma_z(y)\, f(y)\, ds(y),$$

$$\forall\, z \in \mathbb{R}^d \setminus \partial\Omega, \quad \mathcal{D}_\Omega[f](z) = \int_{\partial\Omega} \frac{\partial \Gamma_z(y)}{\partial \nu}\, f(y)\, ds(y).$$

Lemma 9.1.1. *The double layer potential verifies, for all $f \in L^2(\partial\Omega)$,*

$$(-\Delta + k^2)\mathcal{D}_\Omega[f] = 0 \qquad \text{in}\, \mathbb{R}^d \setminus \partial\Omega,$$

$$\frac{\partial}{\partial \nu}\mathcal{D}_\Omega[f]|_+ = \frac{\partial}{\partial \nu}\mathcal{D}_\Omega[f]|_- \qquad \text{on}\, \partial\Omega,$$

$$\mathcal{D}_\Omega[f]|_\pm = \left(\mp\tfrac{1}{2}I + \mathcal{K}_\Omega\right)[f] \qquad \text{on}\, \partial\Omega,$$

where $\mathcal{K}_\Omega : L^2(\partial\Omega) \to L^2(\partial\Omega)$ is defined by

$$\forall\, z \in \partial\Omega, \quad \mathcal{K}_\Omega[f](z) = \int_{\partial\Omega} \frac{\partial}{\nu(\partial y)}\Gamma_z(y) f(y)\, ds(y).$$

Lemma 9.1.2. *Let $d = 2, 3$. The single layer potential verifies, for all $f \in L^2(\partial\Omega)$,*

$$(-\Delta + k^2)\mathcal{S}_\Omega[f] = 0 \qquad \text{in}\, \mathbb{R}^d \setminus \partial\Omega,$$

$$\mathcal{S}_\Omega[f]|_+ = \mathcal{S}_\Omega[f]|_- \qquad \text{on}\, \partial\Omega.$$

The single layer potential is therefore well defined on $\partial\Omega$, and hence on $\mathbb{R}^d$. Moreover,

$$\frac{\partial}{\partial \nu}\mathcal{S}_\Omega[f]|_\pm = \left(\pm\frac{1}{2}I + \mathcal{K}_\Omega^*\right)[f] \qquad \text{on}\, \partial\Omega,$$

where $\mathcal{K}_\Omega^* : L^2(\partial\Omega) \to L^2(\partial\Omega)$ is the L^2-adjoint of the operator $\mathcal{K}_\Omega$, i.e.,

$$\forall\, z \in \partial\Omega, \quad \mathcal{K}_\Omega^*[f](z) = \int_{\partial\Omega} \frac{\partial}{\partial \nu(z)}\Gamma_z(y) f(y)\, ds(y).$$

Let G be the Green function of problem (9.1), that is, for all $z \in \Omega$, the unique solution to

$$\begin{cases} -\Delta_y G_z(y) + k^2\, G_z(y) = \delta_z & \text{in}\, \Omega, \\ \ell \dfrac{\partial G_z}{\partial \nu}(y) + \; G_z(y) = 0 & \text{on}\, \partial\Omega. \end{cases} \tag{9.3}$$

Lemma 9.1.3. *The operator of kernel $G_z(y)$ is the solution operator for problem (9.1):*

$$\forall z \in \Omega, \qquad \Phi_{\text{exc}}^{g}(z) = \frac{1}{\ell} \int_{\partial\Omega} G_z(y) g(y)\, ds(y). \tag{9.4}$$

Proof. Since G_z and Φ_{exc}^{g} are respectively the solutions to problems (9.3) and (9.1), we have the equation

$$\Phi_{\text{exc}}^{g}(z) = \int_{\Omega} \Big[(-\Delta_y G_z(y) + k^2\, G_z(y)) \Phi_{\text{exc}}^{g}(y) - (-\Delta \Phi_{\text{exc}}^{g}(y) + k^2\, \Phi_{\text{exc}}^{g}(y)) G_z(y) \Big]\, dy.$$

Besides, we can apply Green's formula:

$$\begin{aligned} \Phi_{\text{exc}}^{g}(z) &= \int_{\Omega} \Big[-\Delta_y G_z(y) \Phi_{\text{exc}}^{g}(y) + \Delta \Phi_{\text{exc}}^{g}(y) G_z(y) \Big]\, dy \\ &= \int_{\partial\Omega} \Big[-\frac{\partial G_z(y)}{\partial \nu} \Phi_{\text{exc}}^{g}(y) + \frac{\partial \Phi_{\text{exc}}^{g}(y)}{\partial \nu} G_z(y) \Big]\, ds(y). \end{aligned}$$

Using the boundary conditions that G_z and Φ_{exc}^{g} verify, we then obtain that

$$\Phi_{\text{exc}}^{g}(z) = \frac{1}{\ell} \int_{\partial\Omega} G_z(y) g(y)\, ds(y).$$

□

Thanks to the previous lemma, if we know G_z, we can calculate the excitation light fluence for any source g. The following result relates G_z, the Green function of our problem to Γ_z, for which we have an explicit formula. It generalizes [28, Lemma 2.15] to the Green function G_z.

Proposition 9.1.1. *For $z \in \Omega$ and $y \in \partial\Omega$,*

$$\left(-\frac{I}{2} + \mathcal{K}_\Omega + \frac{1}{\ell}\, \mathcal{S}_\Omega \right) [G_z](y) = \Gamma_z(y). \tag{9.5}$$

More precisely, for any simply connected smooth domain D compactly contained in Ω, and for any $h \in L^2(\partial D)$, we have for any $y \in \partial\Omega$:

$$\int_{\partial D} \left(-\frac{I}{2} + \mathcal{K}_\Omega + \frac{1}{\ell}\, \mathcal{S}_\Omega \right) [G_z](y)\, h(z)\, ds(z) = \int_{\partial D} \Gamma_z(y)\, h(z)\, ds(z).$$

Proof. Let $f \in L^2_0(\partial\Omega)$, where $L^2_0(\partial\Omega)$ is the set of L^2 functions in Ω of mean zero. For $z \in \Omega$ and $y \in \partial\Omega$, we define

$$u(z) := \int_{\partial\Omega} \left(-\frac{I}{2} + \mathcal{K}_\Omega + \frac{1}{\ell}\,\mathcal{S}_\Omega\right)[G_z](y) f(y)\,ds(y).$$

By introducing the adjoint operator, we obtain

$$u(z) \;=\; \int_{\partial\Omega} G_z(y)\left(-\frac{I}{2} + \mathcal{K}^*_\Omega + \frac{1}{\ell}\,\mathcal{S}_\Omega\right)[f](y)\,ds(y).$$

By Lemma 9.1.3, u is then a solution to the problem

$$\begin{cases} -\Delta u(y) + k^2\,u(y) = 0 & \text{in}\,\Omega, \\ \dfrac{\partial u}{\partial \nu}(y) + \dfrac{1}{\ell}\,u(y) = \left(-\dfrac{I}{2} + \mathcal{K}^*_\Omega + \dfrac{1}{\ell}\,\mathcal{S}_\Omega\right)[f](y) & \text{on}\,\partial\Omega. \end{cases} \tag{9.6}$$

We know that $\mathcal{S}_\Omega[f]$ is a solution to the problem (9.6), thanks to Lemma 9.1.2. The equation $(-\Delta + k^2)p = 0$ in Ω with the Robin boundary condition, $\partial p/\partial \nu + lp = 0$, admits a unique solution, provided that $l > 0$. Therefore, we have

$$\forall z \in \Omega, \qquad u(z) = \mathcal{S}_\Omega[f](z).$$

Since f is arbitrary, we have therefore proved the first part of our proposition.

Let $h \in L^2(\partial D)$. By multiplying the last equality by h and integrating on ∂D, we obtain

$$\int_{\partial\Omega}\int_{\partial D}\left(-\frac{I}{2} + \mathcal{K}_\Omega + \frac{1}{\ell}\,\mathcal{S}_\Omega\right)[G_z](y)h(z)f(y)\,ds(z)\,ds(y) = \int_{\partial\Omega}\int_{\partial D}\Gamma_z(y)h(z)f(y)\,ds(z)\,ds(y),$$

which completes the proof. □

According to the previous proposition, the knowledge of G_z, and therefore of Φ^g_{exc}, requires the inversion of the operator:

$$-\frac{I}{2} + \mathcal{K}_\Omega + \frac{1}{\ell}\,\mathcal{S}_\Omega : L^2(\partial\Omega) \to L^2(\partial\Omega). \tag{9.7}$$

In the case of circular domains, we can exhibit an explicit formula of the inverse operator.

Explicit calculation of G_z for a circular domain: We assume that the dimension is two and Ω is the unit disk. In terms of polar coordinates, the fundamental solution Γ_z to $-\Delta + k^2$ has the expression:

$$\forall y\,(r,\theta) \in \overline{\Omega},\ \forall z\,(R,\phi) \in \overline{\Omega}, \qquad \Gamma_z(y) = \frac{i}{4}\,H_0^{(1)}(ik|re^{i\theta} - Re^{i\phi}|).$$

Graf's formula [2, Formula (9.1.79)] gives us the following decomposition of Γ_z:

$$H_0^{(1)}(ik|re^{i\theta} - Re^{i\phi}|) = \sum_{m\in\mathbb{Z}} H_m^{(1)}(ikr)J_m(ikR)e^{im(\theta-\phi)}, \quad r > R,$$

with $H_m^{(1)}$ and J_m being respectively the Hankel and Bessel functions of the first kind of order m.

For all $g \in L^2(]0,2\pi[)$, we introduce the Fourier coefficients:

$$\forall m \in \mathbb{Z}, \quad \hat{g}(m) = \frac{1}{2\pi}\int_0^{2\pi} g(\phi)e^{-im\phi}d\phi,$$

and have then

$$g(\phi) = \sum_{m=-\infty}^{\infty} \hat{g}(m)e^{im\phi} \quad \text{in } L^2.$$

Let D be the disk with radius R and center 0. For $y(r,\theta) \in \overline{\Omega}$,

$$\begin{aligned}
\mathcal{S}_D[g](y) &= \frac{iR}{4}\int_0^{2\pi} H_0^{(1)}(ik|re^{i\theta} - Re^{i\phi}|)g(\phi)d\phi, \\
&= \frac{iR}{4}\sum_{m=-\infty}^{\infty} H_m^{(1)}(ikr)J_m(ikR)e^{im\theta}\int_0^{2\pi} g(\phi)e^{-im\phi}d\phi \\
&= \frac{iR\pi}{2}\sum_{m=-\infty}^{\infty} H_m^{(1)}(ikr)J_m(ikR)\hat{g}(m)e^{im\theta}.
\end{aligned}$$

For $y\,(1,\theta) \in \partial\Omega$, we therefore obtain

$$\mathcal{S}_D[g](y) = \sum_{m=-\infty}^{\infty} \widehat{\mathcal{S}_D}(m)\hat{g}(m)e^{im\theta},$$

with

$$\forall m \in \mathbb{Z}, \quad \widehat{\mathcal{S}_D}(m) = \frac{iR\pi}{2}H_m^{(1)}(ik)J_m(ikR),$$

and analogously,

$$\mathcal{S}_\Omega[g](y) = \sum_{m=-\infty}^{\infty} \widehat{\mathcal{S}_\Omega}(m)\hat{g}(m)e^{im\theta},$$

with

$$\forall m \in \mathbb{Z}, \quad \widehat{\mathcal{S}_\Omega}(m) = \frac{i\pi}{2}H_m^{(1)}(ik)J_m(ik).$$

We can prove, in a similar way, that

$$\mathcal{K}_\Omega[g](y) = \sum_{m=-\infty}^{\infty} \widehat{\mathcal{K}_\Omega}(m)\hat{g}(m)e^{im\theta},$$

with

$$\forall m \in \mathbb{Z}, \quad \widehat{\mathcal{K}_\Omega}(m) = \frac{-k\pi}{2}H_m^{(1)}(ik)J_m'(ik).$$

Using Proposition 9.1.1, we can express the Fourier coefficients of the operator with kernel $G_z(y)$ for all $z(R,\theta) \in \partial D$ defined by

$$\int_{\partial\Omega} G_z(y)g(y)\,ds(y) = \sum_{m=-\infty}^{\infty} \widehat{G}(m)\hat{g}(m)e^{im\theta},$$

as follows:

$$\forall m \in \mathbb{Z}, \quad \widehat{G}(m) = \frac{\widehat{\mathcal{S}_D}(m)}{\widehat{\mathcal{K}_\Omega}(m) + \frac{1}{\ell}\widehat{\mathcal{S}_\Omega}(m)},$$

that is,

$$\forall m \in \mathbb{Z}, \quad \widehat{G}(m) = \frac{J_m(ikR)}{ikJ'_m(ik) + \frac{1}{\ell}J_m(ik)}.$$

Moreover, the function Φ^g_{exc} defined by (9.4) can be written as

$$\Phi^g_{\text{exc}}(R,\theta) = \sum_{m=-\infty}^{\infty} \frac{J_m(ikR)}{ik\ell J'_m(ik) + J_m(ik)}\hat{g}(m)e^{im\theta}. \tag{9.8}$$

When Ω is approximated by the unit disk, we have shown that we can easily invert our operator (9.7) and obtain an explicit formula of our Green's function G_z. We can then calculate the excitation light fluence, for any source g, in this particular case. The same result holds for the unit sphere; see Appendix C.

9.2 Expression of c_{flr}

Recall that the concentration of fluorophores c_{flr} can be expressed as

$$c_{\text{flr}} = \delta\,[u]\big|_{\partial C},$$

where δ is a constant and u,the voltage potential in our domain, satisfies (8.4).

Let $L^2_0(\partial C) := \{\Psi \in L^2(\partial C) : \int_{\partial C}\Psi = 0\}$. Let $\Gamma^{(0)}$ be the fundamental solution to Δ in $\mathbb{R}^d$:

$$\Gamma^{(0)}(x) := \begin{cases} \dfrac{1}{2\pi}\log|x|, & d = 2, \\ -\dfrac{1}{4\pi|x|}, & d = 3. \end{cases} \tag{9.9}$$

Analogously to Chapter 9, we introduce the layer potentials, $\mathcal{S}^{(0)}_C, \mathcal{S}^{(0)}_\Omega, \mathcal{D}^{(0)}_C, \mathcal{D}^{(0)}_\Omega, \mathcal{K}^{(0)}_C$, and $(\mathcal{K}^{(0)}_C)^*$ associated with $\Gamma^{(0)}$. The following proposition from [77] gives us a representation formula for the voltage potential in Ω.

Proposition 9.2.1. *There exists at most one solution u to the problem (8.4) and it satisfies the following representation formula:*

$$\forall x \in \Omega, \quad u(x) = H(x) + \mathcal{D}^{(0)}_C[\Psi](x), \tag{9.10}$$

where the harmonic function H is given by

$$\forall x \in \mathbb{R}^2 \setminus \partial\Omega, \quad H(x) = -\mathcal{S}^{(0)}_{\Omega}[g_{\mathrm{ele}}](x) + \mathcal{D}^{(0)}_{\Omega}[u|_{\partial\Omega}](x), \tag{9.11}$$

and $\Psi \in L^2_0(\partial C)$ satisfies the integral equation:

$$\Psi + \beta \frac{\partial \mathcal{D}^{(0)}_C[\Psi]}{\partial \nu} = -\beta \frac{\partial H}{\partial \nu} \quad \text{on } \partial C. \tag{9.12}$$

The decomposition in (9.10) is unique. Furthermore, the following identity holds:

$$\forall x \in \mathbb{R}^2 \setminus \overline{\Omega}, \quad u(x) = H(x) + \mathcal{D}^{(0)}_C[\Psi](x) = 0.$$

Since the normal derivative of the layer potential is continuous across its boundary, the representation formula (9.10) gives us an expression for $\frac{\partial u}{\partial \nu}|_{\partial C}$, and hence for c_{flr} thanks to (8.4) and (8.5). For a given applied electric field g_{ele} and cell C, one can therefore compute the fluorophore concentration c_{flr} on ∂C.

9.3 Expression of Φ^g_{emt}

The emitted light fluence Φ^g_{emt} due to an excitation g is the solution to the following problem:

$$\begin{cases} -\Delta \Phi^g_{\mathrm{emt}}(y) + k^2\, \Phi^g_{\mathrm{emt}}(y) = \dfrac{\tilde{\gamma}}{D}\, c_{\mathrm{flr}}(y)\, \Phi^g_{\mathrm{exc}}(y) & \text{in } \Omega, \\ \ell \dfrac{\partial \Phi^g_{\mathrm{emt}}}{\partial \nu}(y) + \Phi^g_{\mathrm{emt}}(y) = 0 & \text{on } \partial\Omega, \end{cases} \tag{9.13}$$

where Φ^g_{exc} is the excitation light fluence launched by the source g in Ω.

The following result holds.

Theorem 9.3.1. *There exists a unique solution Φ_{emt} in $H^1(\Omega)$ to (9.13).*

Proof. We follow a similar proof as for Φ_{exc} and prove the theorem using Lax-Milgram theory. □

We illustrate with a few numerical simulations the fluorescence forward problem. We take an elliptic domain Ω in which is an elliptic cell C with fluorophores on its membrane. We choose to virtually illuminate our domain with a source $f = 30\cos(2\theta)$. We compute with a finite element method the resulting Φ_{exc} and Φ_{emt} and plot respectively their real and imaginary parts. We consider here that the flourophore concentration is constant over the membrane.

The measured quantity on $\partial\Omega$ is

$$I^g_{\mathrm{emt}} = -D \frac{\partial \Phi^g_{\mathrm{emt}}}{\partial \nu}\bigg|_{\partial\Omega},$$

which is the outgoing light intensity determined from Fick's law. It is worth mentioning that, in our coupled diffusion equations model, if $\ell \neq 0$, then knowing Φ^g_{emt} or $\partial \Phi^g_{\mathrm{emt}}/\partial \nu$ on $\partial\Omega$ is mathematically the same.

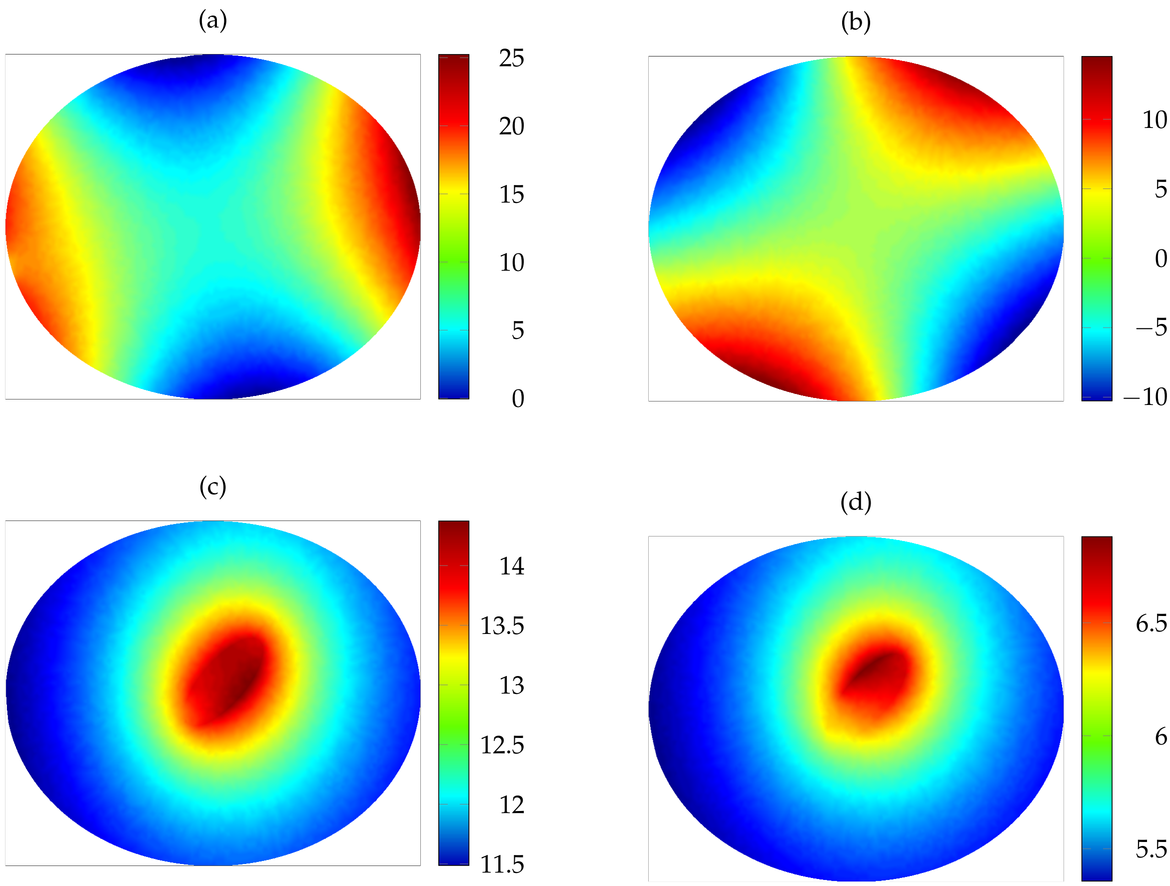

Figure 9.1: *(a) Real part of* Φ_{exc}. *(b) Imaginary part of* Φ_{exc}. *(c) Real part of* Φ_{emt}. *(d) Imaginary part of part of* Φ_{emt}.

Proposition 9.3.1. *The emitted light fluence Φ_{emt}^{g} can be expressed as a function of G_z and Φ_{exc}^{g} as follows:*

$$\forall z \in \overline{\Omega}, \qquad \Phi_{\mathrm{emt}}^{g}(z) = \int_{\partial C} \frac{\tilde{\gamma}}{D}\, G_z(y)\, c_{\mathrm{flr}}(y)\, \Phi_{\mathrm{exc}}^{g}(y)\, ds(y),$$

where ∂C is the cell membrane.

Proof. Since G and Φ_{emt}^{g} are the solutions to the problems (9.3) and (9.13), we have

$$\Phi_{\mathrm{emt}}^{g}(z) - \int_{\Omega} \frac{\tilde{\gamma}}{D}\, G_z(y)\, c_{\mathrm{flr}}(y)\, \Phi_{\mathrm{exc}}^{g}(y)\, dy = \int_{\Omega} \Big[(-\Delta_y G_z(y) + k^2\, G_z(y)) \Phi_{\mathrm{emt}}^{g}(y) - G_z(y)(-\Delta \Phi_{\mathrm{emt}}^{g}(y) + k^2\, \Phi_{\mathrm{emt}}^{g}(y)) \Big]\, dy.$$

Besides, we can apply Green's formula:

$$\Phi_{\mathrm{emt}}^{g}(z) - \int_{\Omega} \frac{\tilde{\gamma}}{D}\, G_z(y)\, c_{\mathrm{flr}}(y)\, \Phi_{\mathrm{exc}}^{g}(y)\, dy = \int_{\partial\Omega} \left[-\frac{\partial G_z(y)}{\partial \nu} \Phi_{\mathrm{emt}}^{g}(y) + G_z(y) \frac{\partial \Phi_{\mathrm{emt}}^{g}(y)}{\partial \nu} \right] ds(y).$$

Using the boundary conditions that G_z and Φ_{emt}^{g} verify, we then obtain

$$\begin{aligned} \Phi_{\mathrm{emt}}^{g}(z) - \int_{\Omega} \frac{\tilde{\gamma}}{D}\, G_z(y)\, c_{\mathrm{flr}}(y)\, \Phi_{\mathrm{exc}}^{g}(y)\, dy &= \int_{\partial\Omega} \left[\frac{1}{\ell} G_z(y) \Phi_{\mathrm{emt}}^{g}(y) + G_z(y) \frac{\partial \Phi_{\mathrm{emt}}^{g}(y)}{\partial \nu} \right] ds(y), \\ &= 0. \end{aligned}$$

Since the concentration of the fluorophores is zero except on ∂C, we get finally the formula:

$$\forall z \in \overline{\Omega}, \qquad \Phi_{\mathrm{emt}}^{g}(z) = \int_{\partial C} \frac{\tilde{\gamma}}{D}\, G_z(y)\, c_{\mathrm{flr}}(y)\, \Phi_{\mathrm{exc}}^{g}(y)\, ds(y).$$

□

By combining the results of the first section and of this last section, for a given concentration of fluorophore c_{flr} and an excitation g, we can express Φ_{emt}^{g}, at any point of $\overline{\Omega}$, and in particular on $\partial\Omega$. Moreover, section 3.2 gives us a unique formula for the fluorophore concentration for given g_{ele} and C. If we couple these two formulas, we solve our forward problem.

Chapter 10

Cell membrane reconstruction

The shape and position of the cell C are now considered to be unknown. We illuminate our domain with a light source g and apply an electric field g_{ele} at its boundary. We measure an outgoing light intensity I^g_{emt}. Our goal is to reconstruct the concentration of fluorophore c_{flr}. We will thus have an image of the membrane potential changes and hence locate the cell. In this section we consider only the two-dimensional case. We start with the reconstruction of the cell membrane ∂C in the case when it is assumed to be a perturbation of a disk. We derive analytical formulas for the resolving power of the proposed imaging method in two different regimes. Then we extend our results to arbitrary shapes. In three dimensions, similar results hold and analytical formulas for the resolving power of the imaging method can be derived for ∂C being a perturbation of a sphere.

10.1 Problem Formulation

The excitation light fluence, Φ^f_{exc}, due to a source $f \in L^2(\partial\Omega)$, is the solution to

$$\begin{cases} -\Delta\Phi^f_{\text{exc}}(y) + k^2\,\Phi^f_{\text{exc}}(y) = 0 & \text{in}\,\Omega, \\ \ell\,\dfrac{\partial\Phi^f_{\text{exc}}}{\partial\nu}(y) + \Phi^f_{\text{exc}}(y) = f & \text{on}\,\partial\Omega. \end{cases}$$

We denote by Φ^g_{exc} the excitation light fluence due to an excitation $g \in L^2(\partial\Omega)$. The emitted light fluence, Φ^g_{emt}, due to the excitation of the fluorophores by Φ^g_{exc}, verifies

$$\begin{cases} -\Delta\Phi^g_{\text{emt}}(y) + k^2\,\Phi^g_{\text{emt}}(y) = \dfrac{\tilde{\gamma}}{D}\,c_{\text{flr}}(y)\,\Phi^g_{\text{exc}}(y) & \text{in}\,\Omega, \\ \ell\,\dfrac{\partial\Phi^g_{\text{emt}}}{\partial\nu}(y) + \Phi^g_{\text{emt}}(y) = 0 & \text{on}\,\partial\Omega. \end{cases}$$

By multiplying the last equation by Φ^f_{exc} and integrating on our domain Ω, we obtain the following formula:

$$\int_\Omega \frac{\tilde{\gamma}}{D}\,c_{\text{flr}}(y)\,\Phi^g_{\text{exc}}(y)\Phi^f_{\text{exc}}(y)\,dy = \int_\Omega \Big[-\Delta\Phi^g_{\text{emt}}(y)\Phi^f_{\text{exc}}(y) + k^2\,\Phi^g_{\text{emt}}(y)\Phi^f_{\text{exc}}(y)\Big]\,dy.$$

From the first equation, we know that in Ω:

$$k^2\,\Phi^f_{\text{exc}}\Phi^g_{\text{emt}} = \Delta\Phi^f_{\text{exc}}\Phi^g_{\text{emt}}.$$

Hence, we have

$$\int_\Omega \frac{\tilde{\gamma}}{D}\,c_{\text{flr}}(y)\,\Phi^g_{\text{exc}}(y)\Phi^f_{\text{exc}}(y)\,dy = \int_\Omega \Big[-\Delta\Phi^g_{\text{emt}}(y)\Phi^f_{\text{exc}}(y) + \Delta\Phi^f_{\text{exc}}(y)\Phi^g_{\text{emt}}(y)\Big]\,dy.$$

Green's formula gives us

$$\int_\Omega \frac{\tilde{\gamma}}{D}\,c_{\text{flr}}(y)\,\Phi^g_{\text{exc}}(y)\Phi^f_{\text{exc}}(y)\,dy = \int_{\partial\Omega} \Big[-\frac{\partial\Phi^g_{\text{emt}}}{\partial\nu}(y)\Phi^f_{\text{exc}}(y) + \frac{\partial\Phi^f_{\text{exc}}}{\partial\nu}(y)\Phi^g_{\text{emt}}(y)\Big]\,ds(y).$$

We use the boundary conditions of our two equations and obtain that

$$\int_\Omega \frac{\tilde{\gamma}}{D}\,c_{\text{flr}}(y)\,\Phi^g_{\text{exc}}(y)\Phi^f_{\text{exc}}(y)\,dy = \frac{1}{\ell}\int_{\partial\Omega} f(y)\,\Phi^g_{\text{emt}}(y)\,ds(y).$$

The concentration of the fluorophores is zero except on ∂C, so we get finally the following proposition.

Proposition 10.1.1. *Let f and g be in $L^2(\partial\Omega)$. The outgoing light intensity $I^g_{\text{emt}} = -D\frac{\partial\Phi^g_{\text{emt}}}{\partial\nu}$ measured on $\partial\Omega$, satisfies the formula:*

$$\int_{\partial C} \tilde{\gamma}\,c_{\text{flr}}(y)\,\Phi^g_{\text{exc}}(y)\Phi^f_{\text{exc}}(y)\,ds(y) = \int_{\partial\Omega} f(y)\,I^g_{\text{emt}}(y)\,ds(y). \tag{10.1}$$

This formula also holds for $\ell = 0$.

For two chosen excitations $f, g \in L^2(\partial\Omega)$ and a measured outgoing light intensity I^g_{emt}, we can compute the integral $\displaystyle\int_{\partial\Omega} f(y)\,I^g_{\text{emt}}(y)\,ds(y)$, and hence, thanks to the last formula, $\displaystyle\int_{\partial C} \tilde{\gamma}\,c_{\text{flr}}(y)\,\Phi^g_{\text{exc}}(y)\Phi^f_{\text{exc}}(y)\,ds(y)$. Recall that the constant $\tilde{\gamma}$ is assumed to be known. Then, if we properly choose f and g, we will be able to reconstruct $c_{\text{flr}}\,\mathbb{1}_{\partial C}$, and therefore to image the cell membrane ∂C.

10.2 Reconstruction of the cell membrane: case of a perturbed disk

We consider a circular cell C with radius R. We choose to excite our medium with a source given by

$$f_n(\phi) = E_n\,e^{in\phi},$$

for $n \in \mathbb{Z}, \phi \in [0, 2\pi]$ and $E_n := ik\ell J_n'(ik) + J_n(ik)$. It gives us, thanks to formula (9.8), the excitation light fluence Φ^n_{exc}:

$$\forall\theta \in [0, 2\pi], \quad \Phi^n_{\text{exc}}(R, \theta) = J_n(ikR)e^{-in\theta}.$$

Let Φ^n_{emt} be the emitted light fluence, and let $I^n_{\mathrm{emt}} = -D\frac{\partial \Phi^n_{\mathrm{emt}}}{\partial \nu}|_{\partial\Omega}$ be the outgoing light intensity measured at $\partial\Omega$ when the cell occupies C and the source f_n is applied at $\partial\Omega$. It follows from (10.1) that

$$\int_{\partial C} \tilde{\gamma} c_{\mathrm{flr}}(\theta)\Phi^n_{\mathrm{exc}}(R,\theta)\Phi^m_{\mathrm{exc}}(R,\theta)Rd\theta = 2\pi\, E_m\, \widehat{I^n_{\mathrm{emt}}}(m). \tag{10.2}$$

Besides, we also have

$$\int_{\partial C} \tilde{\gamma} c_{\mathrm{flr}}(\theta)\Phi^n_{\mathrm{exc}}(R,\theta)\Phi^m_{\mathrm{exc}}(R,\theta)Rd\theta = 2\pi\tilde{\gamma}R\, J_n(ikR)J_m(ikR)\, \widehat{c_{\mathrm{flr}}}(n+m).$$

Let C_ϵ be an ϵ-perturbation of C, *i.e.*, there is $h \in \mathcal{C}^2([0,2\pi])$, such that ∂C_ϵ is given by

$$\partial C_\epsilon = \{\tilde{x};\tilde{x}(\theta) = (R+\epsilon h(\theta))e_r, \theta \in [0,2\pi]\},$$

with (e_r, e_θ) being the basis of polar coordinates.

Our goal is to reconstruct the shape deformation h of our cell. Let $\Phi^n_{\mathrm{emt},\epsilon}$ be the emitted light fluence and let $I^n_{\mathrm{emt},\epsilon} = -D\frac{\partial \Phi^n_{\mathrm{emt},\epsilon}}{\partial \nu}|_{\partial\Omega}$ be the outgoing light intensity measured at the boundary of our domain Ω when the cell occupies C_ϵ and the source f_n is applied at $\partial\Omega$. Again, it follows from (10.1) that

$$\int_{\partial C_\epsilon} \tilde{\gamma}\widetilde{c_{\mathrm{flr}}}(x)\Phi^n_{\mathrm{exc}}(x)\Phi^m_{\mathrm{exc}}(x)\, ds(x) = 2\pi\, E_m\, \widehat{I^n_{\mathrm{emt},\epsilon}}(m). \tag{10.3}$$

On the other hand, we have

$$\int_{\partial C_\epsilon} \tilde{\gamma}\widetilde{c_{\mathrm{flr}}}(x)\Phi^n_{\mathrm{exc}}(x)\Phi^m_{\mathrm{exc}}(x)\, ds(x) = \int_{\partial C} \tilde{\gamma}\widetilde{c_{\mathrm{flr}}}(\tilde{x})\, J_n(ik\tilde{R}(\theta))J_m(ik\tilde{R}(\theta))\, e^{-i(n+m)\theta}ds_\epsilon(\tilde{x}), \tag{10.4}$$

where $\tilde{R}(\theta) = R + \epsilon h(\theta)$ and $\widetilde{c_{\mathrm{flr}}}$ is the concentration of fluorophores on the deformed cell membrane ∂C_ϵ.

We want to compute the first order approximation of our integral (10.4). Taylor-Lagrange's theorem gives us the following expansions, for all $N \in \mathbb{N}$:

$$\begin{aligned} J_m(ik\tilde{R}) &= \sum_{p=0}^{N} \frac{(ik\epsilon h(\theta))^p}{p!} J_m^{(p)}(ikR) + o(\epsilon^N), \\ J_n(ik\tilde{R}) &= \sum_{p=0}^{N} \frac{(ik\epsilon h(\theta))^p}{p!} J_n^{(p)}(ikR) + o(\epsilon^N). \end{aligned} \tag{10.5}$$

In particular, at first order,

$$\begin{aligned} J_m(ik\tilde{R}) &= J_m(ikR) &+\epsilon\, ik\, h(\theta)J'_m(ikR) &+o(\epsilon), \\ J_n(ik\tilde{R}) &= J_n(ikR) &+\epsilon\, ik\, h(\theta)J'_n(ikR) &+o(\epsilon). \end{aligned} \tag{10.6}$$

We can easily get an expansion for the length element $ds_\epsilon(\tilde{y})$, for $\tilde{y} \in \partial C_\epsilon$:

$$ds_\epsilon(\tilde{y}) = |\tilde{x}'(\theta)|d\theta = \Big((R+\epsilon h(\theta))^2 + (\epsilon h'(\theta))^2\Big)^{\frac{1}{2}} d\theta = \sum_{n=0}^{\infty} \epsilon^n \sigma^{(n)}(\theta)d\theta, \tag{10.7}$$

where $\sigma^{(n)}$ are functions bounded independently of n and, at first order, we have

$$ds_\epsilon(\tilde{y}) = Rd\theta + \epsilon h(\theta)d\theta + o(\epsilon). \tag{10.8}$$

10.2.1 High-order terms in the expansion of $\widetilde{c_{\text{flr}}}$

We denote u_ϵ (resp. u) the voltage potential in our medium, when the cell occupies C_ϵ (resp. C). We assume, thanks to (8.5), that our concentration of fluorophores $\widetilde{c_{\text{flr}}}$ (resp. c_{flr}) on ∂C_ϵ (resp. ∂C) is given by

$$\begin{aligned} & \widetilde{c_{\text{flr}}} = \delta\,[u_\epsilon]\big|_{\partial C_\epsilon} \\ \text{resp.} \qquad & c_{\text{flr}} = \delta\,[u]\big|_{\partial C}. \end{aligned}$$

To find the first order term in the expansion of $\widetilde{c_{\text{flr}}}$, we must therefore expand at first u_ϵ. Similar problems have been considered in [40, 41]. Nevertheless, our derivations, based on a layer potential technique, differ significantly from those in [40, 41].

We know, from Proposition 9.2.1, that u_ϵ (resp. u) admits the following representation formula:

$$\begin{aligned} & \forall x \in \Omega, \qquad u_\epsilon(x) = H_\epsilon(x) + \mathcal{D}^{(0)}_{C_\epsilon}[\Psi_\epsilon](x) \\ \text{resp.} \quad & \forall x \in \Omega, \qquad u(x) = H(x) + \mathcal{D}^{(0)}_{C}[\Psi](x), \end{aligned}$$

where the harmonic function H_ϵ (resp. H) is given by

$$\begin{aligned} & \forall x \in \mathbb{R}^2 \setminus \partial\Omega, \qquad H_\epsilon(x) = -\mathcal{S}^{(0)}_{\Omega}[g_{\text{ele}}](x) + \mathcal{D}^{(0)}_{\Omega}[u_\epsilon|_{\partial\Omega}](x) \\ \text{resp.} \quad & \forall x \in \mathbb{R}^2 \setminus \partial\Omega, \qquad H(x) = -\mathcal{S}^{(0)}_{\Omega}[g_{\text{ele}}](x) + \mathcal{D}^{(0)}_{\Omega}[u|_{\partial\Omega}](x), \end{aligned}$$

and $\Psi_\epsilon \in L^2_0(\partial C_\epsilon)$ (resp. $\Psi \in L^2_0(\partial C)$) satisfies the integral equation:

$$\Psi_\epsilon + \beta \frac{\partial \mathcal{D}^{(0)}_{C_\epsilon}[\Psi_\epsilon]}{\partial \tilde{\nu}} = -\beta \frac{\partial H_\epsilon}{\partial \tilde{\nu}} \qquad \text{on}\,\partial C_\epsilon \tag{10.9}$$

$$\text{resp.} \quad \Psi + \beta \frac{\partial \mathcal{D}^{(0)}_{C}[\Psi]}{\partial \nu} = -\beta \frac{\partial H}{\partial \nu} \qquad \text{on}\,\partial C, \tag{10.10}$$

where $\tilde{\nu}(\tilde{x})$ (resp. $\nu(x)$) denotes the outward unit normal to ∂C_ϵ (resp. ∂C) at $\tilde{x}$ (resp. x).

Therefore we obtain, for all $x \in \Omega$,

$$u_\epsilon(x) - u(x) = \mathcal{D}^{(0)}_{\Omega}[u_\epsilon|_{\partial\Omega} - u|_{\partial\Omega}](x) + \mathcal{D}^{(0)}_{C_\epsilon}[\Psi_\epsilon](x) - \mathcal{D}^{(0)}_{C}[\Psi](x),$$

and, on $\partial\Omega$:

$$u_\epsilon(x) - u(x) = (\frac{I}{2} + \mathcal{K}^{(0)}_{\Omega})[u_\epsilon - u](x) + \mathcal{D}^{(0)}_{C_\epsilon}[\Psi_\epsilon](x) - \mathcal{D}^{(0)}_{C}[\Psi](x).$$

Our first step is to find high-order terms in the expansion of Ψ_ϵ. We define the operator $\mathcal{L}_\epsilon$ (resp. $\mathcal{L}$) on $L^2(\partial C_\epsilon)$ (resp. $L^2(\partial C)$) by

$$\begin{aligned} & \mathcal{L}_\epsilon[f] = \frac{\partial \mathcal{D}^{(0)}_{C_\epsilon}[f]}{\partial \tilde{\nu}} \\ \text{resp.} \qquad & \mathcal{L}[f] = \frac{\partial \mathcal{D}^{(0)}_{C}[f]}{\partial \nu}. \end{aligned} \tag{10.11}$$

Proposition 10.2.1. *Let D be a bounded $\mathcal{C}^{2,\eta}$- domain in $\mathbb{R}^2$, for $0 < \eta < 1$. We denote by L_D the normal derivative of the double layer potential on D, $L_D := \partial \mathcal{D}_D^{(0)}/\partial \nu$. Then, $I + \beta L_D : \mathcal{C}^{2,\eta} \to \mathcal{C}^{1,\eta}$ is a bounded operator and has a bounded inverse.*

Proof. The boundedness of $L_D : \mathcal{C}^{2,\eta} \to \mathcal{C}^{1,\eta}$ is proved in [49]. Note that since L_D is not a compact operator, we can not apply the Fredholm alternative. However, L_D is positive [102] and the proposition follows since $\beta > 0$. □

For $f \in \mathcal{C}^{2,\eta}(\partial C_\epsilon)$, $\tilde{x} \in \partial C_\epsilon$, $\mathcal{L}_\epsilon$ has the following expression [77]:

$$\begin{aligned}\frac{\partial \mathcal{D}_{C_\epsilon}^{(0)}[f]}{\partial \nu}(x) = & -\frac{1}{2\pi}\int_{\partial D} \frac{\langle \tilde{\nu}(\tilde{x}), \tilde{\nu}(\tilde{y})\rangle}{|\tilde{x}-\tilde{y}|^2}(f(\tilde{y}) - f(\tilde{x}))\, ds_\epsilon(\tilde{y}) \\ & +\frac{1}{\pi}\int_{\partial D} \frac{\langle \tilde{x}-\tilde{y}, \tilde{\nu}(\tilde{x})\rangle \langle \tilde{x}-\tilde{y}, \tilde{\nu}(\tilde{y})\rangle}{|\tilde{x}-\tilde{y}|^4}(f(\tilde{y}) - f(\tilde{x}))\, ds_\epsilon(\tilde{y}).\end{aligned}$$

The outward unit normal to ∂C at x, $\nu(x)$, and the tangential vector, $T(x)$, are, in terms of polar coordinates:

$$\nu(x) = e_r(x), \quad T(x) = e_\theta(x).$$

The outward unit normal to ∂C_ϵ at $\tilde{x}$, $\tilde{\nu}(\tilde{x})$, is given by

$$\tilde{\nu}(\tilde{x}) = \frac{R_{-\frac{\pi}{2}}(\tilde{x'}(\theta))}{|\tilde{x'}(\theta)|},$$

where $R_{-\frac{\pi}{2}}$ stands for rotation by $-\frac{\pi}{2}$. In our case, we then have

$$\tilde{\nu}(\tilde{x}) = \frac{(R+\epsilon h(\theta))e_r - \epsilon h'(\theta) e_\theta}{((R+\epsilon h(\theta))^2 + (\epsilon h'(\theta))^2)^{\frac{1}{2}}}. \tag{10.12}$$

We can expand $\tilde{\nu}(\tilde{x})$, for $x \in \partial C$, as follows:

$$\tilde{\nu}(\tilde{x}) = \sum_{n=0}^{\infty} \epsilon^n \nu^{(n)}(\theta), \tag{10.13}$$

where the vector-valued functions $\nu^{(n)}$ are uniformly bounded independently of n.

In particular, at first order, $\tilde{\nu}(\tilde{x})$ for $\tilde{x} \in \partial C_\epsilon$ is given by

$$\tilde{\nu}(\tilde{x}) = e_r - \frac{h'(\theta)}{R}\, e_\theta + o(\epsilon). \tag{10.14}$$

Set $\tilde{x}, \tilde{y} \in \partial C_\epsilon$. We have

$$\tilde{x} - \tilde{y} = R(e_r(x) - e_r(y)) + \epsilon(h(\theta^x)\, e_r(x) - h(\theta^y)\, e_r(y)). \tag{10.15}$$

If we denote

$$c = \cos(\theta^x - \theta^y), \quad s = \sin(\theta^x - \theta^y), \tag{10.16}$$

then we obtain

$$|\tilde{x}-\tilde{y}|^2 = 2R^2(1-c) + \quad 2\epsilon R(1-c)(h(\theta^x)+h(\theta^y)) \\ +\epsilon^2\left(h(\theta^x)^2+h(\theta^y)^2-2h(\theta^x)h(\theta^y)c\right).$$

and

$$\frac{1}{|\tilde{x}-\tilde{y}|^2} = \frac{1}{2R^2(1-c)}\,\frac{1}{1+\epsilon F(\theta^x,\theta^y)+\epsilon^2 G(\theta^x,\theta^y)}, \tag{10.17}$$

where

$$F(\theta^x,\theta^y) = \frac{(h(\theta^x)+h(\theta^y))}{R}, \quad G(\theta^x,\theta^y) = \frac{\langle h(\theta^x)\,e_r(x)-h(\theta^y)\,e_r(y)\rangle^2}{2R^2(1-c)}.$$

Likewise, we write

$$\frac{1}{|\tilde{x}-\tilde{y}|^4} = \frac{1}{4R^4(1-c)^2}\,\frac{1}{(1+\epsilon F(\theta^x,\theta^y)+\epsilon^2 G(\theta^x,\theta^y))^2}. \tag{10.18}$$

It follows, from (10.12), (10.7) and (10.17), that

$$\frac{\langle\tilde{\nu}(\tilde{x}),\tilde{\nu}(\tilde{y})\rangle}{|\tilde{x}-\tilde{y}|^2}\,ds_\epsilon(\tilde{y}) = \frac{K_0+\epsilon K_1+\epsilon^2 K_2}{2R^2(1-c)} \\ \times\frac{1}{1+\epsilon F(\theta^x,\theta^y)+\epsilon^2 G(\theta^x,\theta^y)}\,\frac{R}{((R+\epsilon h(\theta^x))^2+(\epsilon h'(\theta^x))^2)^{\frac{1}{2}}}Rd\theta^y,$$

where

$$K_0 = c,$$

$$K_1 = \frac{1}{R}\left[(h(\theta^x)+h(\theta^y))c+(h'(\theta^x)-h'(\theta^y))s\right],$$

$$K_2 = \frac{h'(\theta^x)h'(\theta^y)}{R^2}c.$$

One can see, from the previous formulas, that the singularity of $\dfrac{K_i}{2R^2(1-c)}$ for $i\in[0,2]$ is of order $O(|\theta^x-\theta^y|^{-2})$, since $1-c=O(|\theta^x-\theta^y|^{-2})$.

Likewise, thanks to (10.12), (10.7) and (10.17), we can explicit M_i for $i\in[0,4]$ such that

$$\frac{\langle\tilde{x}-\tilde{y},\tilde{\nu}(\tilde{x})\rangle\langle\tilde{x}-\tilde{y},\tilde{\nu}(\tilde{y})\rangle}{|\tilde{x}-\tilde{y}|^4}\,ds_\epsilon(\tilde{y}) = \frac{M_0+\epsilon M_1+\epsilon^2 M_2+\epsilon^3 M_3+\epsilon^4 M_4}{4R^4(1-c)^2} \\ \times\frac{1}{(1+\epsilon F(\theta^x,\theta^y)+\epsilon^2 G(\theta^x,\theta^y))^2}\,\frac{R}{((R+\epsilon h(\theta^x))^2+(\epsilon h'(\theta^x))^2)^{\frac{1}{2}}}Rd\theta^y,$$

and the singularity of $\dfrac{M_i}{4R^4(1-c)^2}$ for $i \in [0,4]$ is of order $O(|\theta^x - \theta^y|^{-2})$. Therefore, we get

$$\begin{aligned} L_\epsilon \, ds_\epsilon(\tilde{y}) = & \frac{N_0 + \epsilon N_1 + \epsilon^2 N_2 + \epsilon^3 N_3 + \epsilon^4 N_4}{2R^4(1-c)^2} \\ & \times \frac{1}{(1+\epsilon F(\theta^x,\theta^y) + \epsilon^2 G(\theta^x,\theta^y))^2} \frac{R}{((R+\epsilon h(\theta^x))^2 + (\epsilon h'(\theta^x))^2)^{\frac{1}{2}}} R d\theta^y, \end{aligned}$$

where $L_\epsilon := -\dfrac{\langle \tilde{\nu}(\tilde{x}), \tilde{\nu}(\tilde{y})\rangle}{|\tilde{x}-\tilde{y}|^2} + 2\dfrac{\langle \tilde{x}-\tilde{y}, \tilde{\nu}(\tilde{x})\rangle \langle \tilde{x}-\tilde{y}, \tilde{\nu}(\tilde{y})\rangle}{|\tilde{x}-\tilde{y}|^4}$ is the kernel of $\mathcal{L}_\epsilon$ and the singularity of $\dfrac{N_i}{2R^4(1-c)^2}$ for $i \in [0,4]$ is of order $O(|\theta^x - \theta^y|^{-2})$. We do not give here the expressions of N_2, N_3, N_4 due to their length, but N_0 and N_1 are given by

$$\begin{aligned} N_0 &= -R^2(1-c), \\ N_1 &= -2R(1-c)(h(\theta^x) + h(\theta^y)). \end{aligned}$$

Recall that

$$F(\theta^x,\theta^y) = \frac{(h(\theta^x) + h(\theta^y))}{R}, \quad G(\theta^x,\theta^y) = \frac{(h(\theta^x) - h(\theta^y)^2 + 2h(\theta^x)h(\theta^y)(1-c)}{2R^2(1-c)}.$$

We introduce the following series, which converges absolutely and uniformly,

$$\frac{1}{(1+\epsilon F(\theta^x,\theta^y) + \epsilon^2 G(\theta^x,\theta^y))^2} \frac{R}{((R+\epsilon h(\theta^x))^2 + (\epsilon h'(\theta^x))^2)^{\frac{1}{2}}} = \sum_{p=0}^{\infty} \epsilon^p F_p(\theta^x,\theta^y).$$

The first order term is given by

$$F_1(\theta^x,\theta^y) = -\frac{(3h(\theta^x) + 2h(\theta^y))}{R}. \tag{10.19}$$

Note that $(F_p)_{p\in\mathbb{N}}$, like F and G, have no singularity and are uniformly bounded.

We define the following functions, for all $x, y \in \partial C$:

$$L^{(0)} = \frac{N_0}{2R^4(1-c)^2}, \qquad L^{(1)} = \frac{N_0 F_1 + N_1}{2R^4(1-c)^2},$$

$$L^{(2)} = \frac{N_0 F_2 + N_1 F_1 + N_2}{2R^4(1-c)^2}, \qquad L^{(3)} = \frac{N_0 F_3 + N_1 F_2 + N_2 F_1 + N_3}{2R^4(1-c)^2},$$

and, for $n \geq 4$,

$$L^{(n)} = \frac{1}{2R^4(1-c)^2}\left(N_0 F_n + N_1 F_{n-1} + N_2 F_{n-2} + N_3 F_{n-3} + N_4 F_{n-4}\right). \tag{10.20}$$

Thanks to the explicit formulas of $(N_i)_{i\in[0,4]}$ and (10.19), we obtain in particular that, for all $x, y \in \partial C$,

$$L^{(0)} = -\frac{1}{2R^3(1-c)} \quad \text{and} \quad L^{(1)} = \frac{h(\theta^x)}{2R^3(1-c)}, \tag{10.21}$$

where c is given by (10.16).

By construction, $L^{(n)}$, for all $n \in \mathbb{N}$, have a singularity of order $O(|\theta^x - \theta^y|^{-2})$.

The integral operators $(\mathcal{L}^{(n)})_{n\in\mathbb{N}}$, associated to the kernels $(L^{(n)})_{n\in\mathbb{N}}$, are given, for all $f \in \mathcal{C}^{2,\eta}(\partial C)$, $x \in \partial C$, by

$$\mathcal{L}^{(n)}[f](x) = \frac{1}{2\pi}\int_0^{2\pi} L^{(n)}(\theta^x, \theta^y)(f(\theta^y) - f(\theta^x))Rd\theta^y.$$

It follows from (10.21) that, for all $\mathcal{C}^{2,\eta}(\partial C)$, $x \in \partial C$:

$$\mathcal{L}^{(0)}[f](x) = \mathcal{L}[f](x) \quad \text{and} \quad \mathcal{L}^{(1)}[f](x) = -h(\theta^x)\mathcal{L}[f](x). \tag{10.22}$$

We can now write, from our construction, an expansion of $\mathcal{L}_\epsilon$.

Proposition 10.2.2. *Let $N \in \mathbb{N}$. There exists C depending only on R and $||h||_{\mathcal{C}^2}$, such that, for any $\tilde{f} \in \mathcal{C}^{2,\eta}(\partial C_\epsilon)$, $0 < \eta < 1$, we have*

$$||\mathcal{L}_\epsilon[\tilde{f}] \circ \tau_\epsilon - \mathcal{L}[f] - \sum_{n=0}^{N} \epsilon^n \mathcal{L}^{(n)}[f]||_{\mathcal{C}^{1,\eta}(\partial C)} \le C\epsilon^{N+1}||f||_{\mathcal{C}^{2,\eta}(\partial C)},$$

where τ_ϵ is the diffeomorphism from ∂C onto ∂C_ϵ given by $\tau_\epsilon(x) = \tilde{x}$ and the function f is defined by $f := \tilde{f} \circ \tau_\epsilon$.

Proof. Let $f \in \mathcal{C}^{2,\eta}$. We know that $\dfrac{N_i}{2R^4(1-c)^2}$, for all $i \in [0,4]$, have a singularity of order $O(|\theta^x - \theta^y|^{-2})$.

Thanks to the $\mathcal{C}^1$-character of f, $(\theta^x, \theta^y) \to \dfrac{N_i}{2R^4(1-c)^2}(f(\theta^y) - f(\theta^x))$ have a singularity of order $O(|\theta^x - \theta^y|^{-1})$.

Besides the Hilbert transform is a bounded operator from $\mathcal{C}^{0,\eta}$ to $\mathcal{C}^{0,\eta}$. From the boundedness of h and its derivatives, it follows that the operators associated with the kernels $\dfrac{N_i}{2R^4(1-c)^2}$ for $i \in [0,4]$ are bounded from $\mathcal{C}^{2,\eta}$ to $\mathcal{C}^{1,\eta}$.

Since the $(F_p)_{p\in\mathbb{N}}$ are uniformly bounded, the construction of $L^{(n)}$ (10.20) implies that there exists a constant $K(R, ||h||_{\mathcal{C}^2})$ such that

$$||\mathcal{L}^{(n)}[f]||_{\mathcal{C}^{0,\eta}(\partial C)} \le K||f'||_{\mathcal{C}^{0,\eta}(\partial C)},$$

where f' is the derivative of f with respect to θ. Likewise, since the kernel of $\mathcal{L}^{(n)}[f]'(x)$ is of order $O\left(\dfrac{f(y) - f(x) - (x-y)f'(x)}{|x-y|^2}\right)$, the $\mathcal{C}^2$-character of f gives us a singularity of order $O(|\theta^x - \theta^y|^{-1})$. We therefore obtain that

$$||\mathcal{L}^{(n)}[f]'||_{\mathcal{C}^{0,\eta}(\partial C)} \le \tilde{K}||f''||_{\mathcal{C}^{0,\eta}(\partial C)},$$

where $\tilde{K}(R, ||h||_{\mathcal{C}^2})$ is a constant and f'' is the second derivative of f. Therefore, there exists a constant $\widehat{K}(R, ||h||_{\mathcal{C}^2})$ such that

$$||\mathcal{L}^{(n)}[f]||_{\mathcal{C}^{1,\eta}(\partial C)} \leq \widehat{K}||f||_{\mathcal{C}^{2,\eta}(\partial C)}.$$

For all $n \in \mathbb{N}$, the operator $\mathcal{L}^{(n)} : \mathcal{C}^{2,\eta} \to \mathcal{C}^{1,\eta}$ is bounded and the constant $\widehat{K}$ does not depend on n. Let $N \in \mathbb{N}$. Let $\tilde{f} \in \mathcal{C}^{2,\eta}(\partial C_\epsilon)$. We introduce $f := \tilde{f} \circ \tau_\epsilon$, $f \in \mathcal{C}^{2,\eta}(\partial C)$. We have

$$|| \sum_{n=N+1}^{\infty} \epsilon^n \mathcal{L}^{(n)}[f]||_{\mathcal{C}^{1,\eta}(\partial C)} \leq \frac{\epsilon^{N+1}}{1-\epsilon} \widehat{K}\, ||f||_{\mathcal{C}^{2,\eta}(\partial C)},$$

which ends the proof of the result. □

By substituting the result of Proposition 10.2.2 into the integral equation (10.9) verified by Ψ_ϵ, we obtain for all $N \in \mathbb{N}$ that

$$\forall x \in \partial C, \;\; (I + \beta\mathcal{L} + \beta \sum_{n=0}^{N} \epsilon^n \mathcal{L}^{(n)})[\Psi_\epsilon](\tilde{x}) + o(\epsilon^N) = -\beta \frac{\partial H_\epsilon}{\partial \tilde{\nu}}(\tilde{x}). \tag{10.23}$$

We use Taylor-Lagrange's theorem and (10.13) to expand $\frac{\partial H_\epsilon}{\partial \tilde{\nu}}(\tilde{x})$:

$$\frac{\partial H_\epsilon}{\partial \tilde{\nu}}(\tilde{x}) = \left(\sum_{p=0}^{\infty} \sum_{|\alpha|=p} \frac{\epsilon^p}{\alpha!} (\partial^\alpha \nabla H_\epsilon)(x)(h(\theta)\nu(x))^\alpha \right) \left(\sum_{p=0}^{\infty} \epsilon^p \nu^{(p)}(\theta) \right). \tag{10.24}$$

In particular, at first order, we have

$$\frac{\partial H_\epsilon}{\partial \tilde{\nu}}(\tilde{x}) = \frac{\partial H_\epsilon}{\partial r}(x) + \epsilon \left(-\frac{h'(\theta)}{R^2} \frac{\partial H_\epsilon}{\partial \theta}(x) + h(\theta) \frac{\partial^2 H_\epsilon}{\partial r^2}(x) \right). \tag{10.25}$$

Our integral equation (10.23) then becomes

$$\forall x \in \partial C, \;\; (I + \beta\mathcal{L} + \beta \sum_{p=0}^{N} \epsilon^n \mathcal{L}^{(n)})[\Psi_\epsilon](\tilde{x}) + o(\epsilon^N) = -\beta \sum_{n=0}^{\infty} \epsilon^n G_n(x), \tag{10.26}$$

where $(G_n)_{n \in \mathbb{N}}$ are the coefficients in the expansion (10.24).
Equation (10.26) can therefore be solved recursively in the following way:

$$\begin{aligned} &\Psi^{(0)} = -\beta(I + \beta\mathcal{L})^{-1} [G_0], \\ \forall n \leq N, \qquad &\Psi^{(n)} = -\beta(I + \beta\mathcal{L})^{-1} \left[G_n + \sum_{p=0}^{n-1} \mathcal{L}^{(n-p)} \Psi^{(p)} \right]. \end{aligned} \tag{10.27}$$

In particular, thanks to (10.22) and (10.25), we have

$$\begin{aligned} \Psi^{(0)} &= -\beta(I + \beta\mathcal{L})^{-1} \left(\frac{\partial H_\epsilon}{\partial \nu} \right), \\ \Psi^{(1)} &= -\beta(I + \beta\mathcal{L})^{-1} \left(-\frac{h'}{R^2} \frac{\partial H_\epsilon}{\partial \theta} + h \frac{\partial^2 H_\epsilon}{\partial r^2} - h \frac{\partial}{\partial \nu} \mathcal{D}_C^{(0)}[\Psi^{(0)}] \right). \end{aligned} \tag{10.28}$$

We obtain the following proposition.

Proposition 10.2.3. *Let $N \in \mathbb{N}$. There exists K, depending only on N, R and the $\mathcal{C}^2$- norm of h, such that*

$$||\Psi_\epsilon - \sum_{n=0}^{N} \epsilon^n \Psi^{(n)}||_{\mathcal{C}^{2,\eta}(\partial C)} \leq K\epsilon^{N+1}, \tag{10.29}$$

where $(\Psi^{(n)})_{n\leq N}$ are defined by the recursive relation (10.27).

In order to prove Proposition 10.2.3, we need the following result [74, Theorem 1.16].

Lemma 10.2.1. *Let X and Y be two Banach spaces. Let T and A be two operators from X to Y, such that $D(T) \subset D(A)$, where $D(T)$ and $D(A)$ are the domains of T and A, respectively. Let T^{-1} exist and be a bounded operator from Y to X (so that T is closed). We suppose that two positive constants a, b exist such that*

$$\forall u \in D(T), \quad ||Au|| \leq a||u|| + b||Tu||,$$
$$a||T^{-1}|| + b < 1.$$

Then $S = T + A$ is closed and invertible, S^{-1} is a bounded operator from Y to X and the following inequalities hold:

$$||S^{-1}|| \leq \frac{||T^{-1}||}{1 - a||T^{-1}|| - b}, \quad ||S^{-1} - T^{-1}|| \leq \frac{||T^{-1}||(a||T^{-1}|| + b)}{1 - a||T^{-1}|| - b}.$$

If in addition T^{-1} is compact, then so is S^{-1}.

Proof of Proposition 10.2.3. By definition, Ψ_ϵ verifies:

$$(I + \beta\mathcal{L}_\epsilon)[\Psi_\epsilon] = -\beta \sum_{n=0}^{\infty} \epsilon^n G_n.$$

Besides, it follows, from our recursive construction of the $(\Psi^{(i)})_{i\in[0,N]}$, that

$$(I + \beta\mathcal{L} + \beta \sum_{n=1}^{N} \epsilon^n \mathcal{L}^{(n)})[\sum_{n=0}^{N} \epsilon^p \Psi^{(p)}] = -\beta \sum_{n=0}^{\infty} \epsilon^n G_n + \epsilon^{N+1} A_N,$$

where $A_N = \sum_{n=0}^{N} \epsilon^n \sum_{p=0}^{N+n} \mathcal{L}^{(N+1+n-p)} [\Psi^{(p)}] + \beta \sum_{n=0}^{\infty} \epsilon^n G_{N+1+n}$.

Therefore, we have

$$\begin{aligned}\Psi_\epsilon - \sum_{n=0}^{N} \epsilon^n \Psi^{(n)} = \quad & \left((I + \beta\mathcal{L}_\epsilon)^{-1} - (I + \beta\mathcal{L} + \beta \sum_{n=1}^{N} \epsilon^n \mathcal{L}^{(n)})^{-1} \right) [-\beta \sum_{n=0}^{\infty} \epsilon^n G_n] \\ & -(I + \beta\mathcal{L} + \beta \sum_{n=1}^{N} \epsilon^n \mathcal{L}^{(n)})^{-1} [\epsilon^{N+1} A_N].\end{aligned} \tag{10.30}$$

We know from Proposition 10.2.1 that the bounded operator $T := I + \beta\mathcal{L}_\epsilon : \mathcal{C}^{2,\eta} \to \mathcal{C}^{1,\eta}$ has a bounded inverse $T^{-1} : \mathcal{C}^{1,\eta} \to \mathcal{C}^{2,\eta}$. We define

$$A := \beta\mathcal{L} + \beta \sum_{n=1}^{N} \epsilon^n \mathcal{L}^{(n)} - \beta\mathcal{L}_\epsilon.$$

From Proposition 10.2.2, it follows that there exists a constant $C(R, ||h||_{\mathcal{C}^2})$ such that

$$||A[u]||_{\mathcal{C}^{1,\eta}(\partial C)} \leq C\epsilon^{N+1} ||u||_{\mathcal{C}^{2,\eta}(\partial C)}.$$

For ϵ small enough, we have

$$C\epsilon^{N+1}||T^{-1}|| < 1.$$

In the following, we apply Lemma 10.2.1 with $a := C\,\epsilon^{N+1}$ and $b := 0$.

The operator $S := I + \beta\mathcal{L} + \beta \sum_{n=1}^{N} \epsilon^n \mathcal{L}^{(n)}$ has a bounded inverse, which satisfies:

$$||(I + \beta\mathcal{L} + \beta \sum_{n=1}^{N} \epsilon^n \mathcal{L}^{(n)})^{-1}|| \leq \frac{||T^{-1}||}{1 - C\epsilon^{N+1}||T^{-1}||},$$

and $$||(I + \beta\mathcal{L} + \beta \sum_{n=1}^{N} \epsilon^n \mathcal{L}^{(n)})^{-1} - (I + \beta\mathcal{L}_D)^{-1}|| \leq \frac{C\epsilon^{N+1}||T^{-1}||^2}{1 - C\epsilon^{N+1}||T^{-1}||}.$$

We use (10.30) to get

$$\left|\left|\Psi_\epsilon - \sum_{n=0}^{N} \epsilon^n\, \Psi^{(n)}\right|\right|_{\mathcal{C}^{2,\eta}} \leq \frac{\epsilon^{N+1}||T^{-1}||}{1 - C\epsilon^{N+1}||T^{-1}||} \left(C||T^{-1}|| \left|\left|\beta \frac{\partial H_\epsilon}{\partial \tilde{\nu}}\right|\right|_{\mathcal{C}^{1,\eta}} + ||A_N||_{\mathcal{C}^{1,\eta}} \right).$$

Recall that H_ϵ is $\mathcal{C}^\infty$ on ∂C. Hence, for all $p \in \mathbb{N}$, G_p is bounded. From Proposition 10.2.2, we know that $\mathcal{L}^{(n)} : \mathcal{C}^{2,\eta}(\partial C) \to \mathcal{C}^{1,\eta}(\partial C)$, for all $n \in \mathbb{N}$, are bounded operators. We have also, from Proposition 10.2.1, that $(I + \beta\mathcal{L})^{-1} : \mathcal{C}^{1,\eta}(\partial C) \to \mathcal{C}^{2,\eta}(\partial C)$ is bounded. One can prove recursively, from the construction (10.29), that, for all $p \in \mathbb{N}$, $\Psi^{(p)}$ is $\mathcal{C}^{2,\eta}(\partial C)$ - bounded. A_N and $\dfrac{\partial H_\epsilon}{\partial \tilde{\nu}}$ are therefore $\mathcal{C}^{1,\eta}(\partial C)$ - bounded.

Finally, we obtain that there exists a constant $K(N, R, ||h||_{\mathcal{C}^2})$ such that

$$\left|\left|\Psi_\epsilon - \sum_{n=0}^{N} \epsilon^n\, \Psi^{(n)}\right|\right|_{\mathcal{C}^{2,\eta}} \leq K\,\epsilon^{N+1},$$

and the proof of Proposition 10.2.3 is complete. □

We now explicit the first order term in the expansion of $\widetilde{c_{\text{flr}}}$ as function of the cell membrane perturbation. For doing so, we introduce, for $n \in \mathbb{N} \setminus \{0\}$ and $x \in \partial\Omega$:

$$v_n(x) := \sum_{i+j+k+l=n} \int_0^{2\pi} \frac{h(y)^i}{i!} \left(\nabla_y \Big(\frac{\partial^i}{\partial r_y^i} \Gamma^{(0)}(x,y) \Big) \cdot \nu^{(j)}(y) \right) \Psi^{(k)}(\theta^y) \sigma^{(l)}(\theta^y) d\theta^y. \tag{10.31}$$

It follows from (10.8), (10.14), (10.29) and (10.31), that for all $x \in \partial\Omega$:

$$\begin{aligned} v_1(x) = & \int_0^{2\pi} \frac{\partial^2}{\partial r_y^2}\Gamma^{(0)}(x,y)h(\theta^y)\Psi^{(0)}(\theta^y)Rd\theta^y \quad -\frac{1}{R}\int_0^{2\pi} \frac{\partial}{\partial \theta^y}\Gamma^{(0)}(x,y)\Psi^{(0)}(\theta^y)h'(\theta^y)d\theta^y \\ + & \int_0^{2\pi} \frac{\partial}{\partial r_y}\Gamma^{(0)}(x,y)\Psi^{(1)}(\theta^y)Rd\theta^y \quad + \int_0^{2\pi} \frac{\partial}{\partial r_y}\Gamma^{(0)}(x,y)\Psi^{(0)}(\theta^y)h(\theta^y)d\theta^y. \end{aligned}$$

In terms of polar coordinates, the Laplacian has the following expression:

$$\Delta = \frac{\partial^2}{\partial r^2} + \frac{1}{r}\frac{\partial}{\partial r} + \frac{1}{r^2}\frac{\partial^2}{\partial \theta^2}.$$

Therefore, we have for all $x \in \partial\Omega$:

$$\begin{aligned} v_1(x) = & -\frac{1}{R}\int_0^{2\pi} \frac{\partial^2}{\partial \theta^{y2}}\Gamma^{(0)}(x,y)h(\theta^y)\Psi^{(0)}(\theta^y)d\theta^y - \frac{1}{R}\int_0^{2\pi} \frac{\partial}{\partial \theta^y}\Gamma^{(0)}(x,y)\Psi^{(0)}(\theta^y)h'(\theta^y)d\theta^y \\ + & \int_0^{2\pi} \frac{\partial}{\partial r_y}\Gamma^{(0)}(x,y)\Psi^{(1)}(\theta^y)Rd\theta^y. \end{aligned}$$

Besides, we obtain, thanks to (10.29) and (10.31), that

$$\mathcal{D}^{(0)}_{C_\epsilon}[\Psi_\epsilon](x) = -\beta\,\mathcal{D}^{(0)}_{C}(I+\beta\mathcal{L})^{-1}\left[\frac{\partial H_\epsilon}{\partial \nu}\bigg|_{\partial C}\right] + \sum_{n=1}^{N}\epsilon^n v_n(x) + o(\epsilon^N).$$

The integral equation (10.10) that Ψ verifies, then gives us

$$\mathcal{D}^{(0)}_{C_\epsilon}[\Psi_\epsilon] - \mathcal{D}^{(0)}_{C}[\Psi] = -\beta\,\mathcal{D}^{(0)}_{C}(I+\beta\mathcal{L})^{-1}\left[\frac{\partial H_\epsilon}{\partial \nu}\bigg|_{\partial C} - \frac{\partial H}{\partial \nu}\bigg|_{\partial C}\right] + \sum_{n=1}^{N}\epsilon^n v_n + o(\epsilon^N).$$

By definition, we have on ∂C

$$H_\epsilon - H = \mathcal{D}^{(0)}_{\Omega}[u_\epsilon|_{\partial\Omega} - u|_{\partial\Omega}].$$

Let $\mathcal{E}$ be the operator defined by

$$\mathcal{E}[v](x) := \beta\,\mathcal{D}^{(0)}_{C}(I+\beta\mathcal{L})^{-1}\left[\frac{\partial}{\partial \nu}(\mathcal{D}^{(0)}_{\Omega}v)\bigg|_{\partial C}\right](x) - (\frac{I}{2} + \mathcal{K}^{(0)}_{\Omega})[v](x), \qquad (10.32)$$

for all $v \in L^2_0(\partial\Omega)$ and $x \in \partial\Omega$.

Recall that on $\partial\Omega$:

$$u_\epsilon(x) - u(x) = (\frac{I}{2} + \mathcal{K}^{(0)}_{\Omega})[u_\epsilon - u](x) + \mathcal{D}^{(0)}_{C_\epsilon}[\Psi_\epsilon](x) - \mathcal{D}^{(0)}_{C}[\Psi](x).$$

We obtain, for all $x \in \partial\Omega$, that

$$(I+\mathcal{E})[u_\epsilon - u](x) = \sum_{n=1}^{N}\epsilon^n v_n(x) + o(\epsilon^N), \qquad (10.33)$$

and, at first order,
$$(I+\mathcal{E})[u_\epsilon - u](x) = \epsilon\, v_1(x) + o(\epsilon),$$
where v_1 is given by the formula:
$$v_1(x) = -\frac{1}{R}\int_0^{2\pi} \frac{\partial}{\partial\theta^y}\left(h(\theta^y)\frac{\partial}{\partial\theta^y}\Gamma^{(0)}(x,y)\right)\Psi^{(0)}(\theta^y)d\theta^y + \mathcal{D}_C^{(0)}[\Psi^{(1)}](x). \quad (10.34)$$

Proposition 10.2.4. *Let $\mathcal{E}$ be defined by (10.32). The operator $I+\mathcal{E}$ is invertible on $L^2_0(\partial\Omega)$.*

Proof. The operator $\mathcal{E}$ is compact. We can therefore apply the Fredholm alternative. Let us prove the injectivity of $I+\mathcal{E}$. For doing so, we introduce the function v defined on Ω by
$$v(x) = \mathcal{D}_\Omega^{(0)}[v|_{\partial\Omega}] - \beta\,\mathcal{D}_C^{(0)}(I+\beta\mathcal{L})^{-1}\left[\frac{\partial}{\partial\nu}(\mathcal{D}_\Omega^{(0)}[v])\bigg|_{\partial C}\right].$$
It follows from Proposition 9.2.1 that v is solution to (8.4) with $H = \mathcal{D}_\Omega^{(0)}[v|_{\partial\Omega}]$. The decomposition of the representation formula of such a solution is unique so that we have $\mathcal{S}_\Omega^{(0)}[\frac{\partial v}{\partial\nu}|_{\partial\Omega}] = 0$ and hence $\frac{\partial v}{\partial\nu}\Big|_{\partial\Omega} = 0$. Since v is harmonic, we obtain that v is constant in Ω. Recall that $\int_{\partial\Omega} v = 0$. Therefore, we have $v = 0$ in Ω. Besides, on $\partial\Omega$, v verifies:
$$\forall x \in \partial\Omega, \qquad v(x) = -\mathcal{E}[v](x).$$
We have proved the injectivity and hence invertibility of $I+\mathcal{E}$ on $L^2_0(\partial\Omega)$. $\square$

Now, combining Proposition 10.2.4 and (10.33) yields
$$u_\epsilon(x) - u(x) = \sum_{n=1}^{N} \epsilon^n (I+\mathcal{E})^{-1}[v_n](x) + o(\epsilon^N).$$

Note that by construction $\Psi^{(n)}$ and thus v_n still depend on ϵ. We can remove this dependence from our asymptotic formula in the following way. We introduce $(G_n^0)_{n\in\mathbb{N}}$ the expansion of $\frac{\partial H}{\partial\tilde\nu}$. Let $(v_n^0)_{n\in\mathbb{N}\setminus\{0\}}$ and $(\Psi_0^{(n)})_{n\in\mathbb{N}}$ be defined by (10.31) and (10.27), where $(G_n)_{n\in\mathbb{N}}$ is replaced respectively by $(G_n^0)_{n\in\mathbb{N}}$. We then obtain that
$$\forall x \in \partial C, \qquad \Psi_\epsilon(x) = \Psi_0^{(0)}(x) + o(1),$$
$$\forall x \in \partial\Omega, \qquad u_\epsilon(x) = u(x) + o(1).$$
By repeating the same procedure with $H + \epsilon\,\mathcal{D}_\Omega^{(0)}(I+\mathcal{E})^{-1}[v_1^0]$ instead of H, one finds $(v_n^1)_{n\in\mathbb{N}^*}$ and $(\Psi_1^{(n)})_{n\in\mathbb{N}}$ such that
$$\forall x \in \partial C, \qquad \Psi_\epsilon(x) = \Psi_1^{(0)}(x) + \epsilon\,\Psi_1^{(1)}(x) + o(\epsilon),$$
$$\forall x \in \partial\Omega, \qquad u_\epsilon(x) = u(x) + \epsilon(I+\mathcal{E})^{-1}[v_1^1] + o(\epsilon).$$

One can prove the following proposition, by repeating the same procedure until one obtains $(v_n^N)_{n\in\mathbb{N}\setminus\{0\}}$.

Proposition 10.2.5. *Let $(v_n^N)_{n\in[1,N]}$ and $(\Psi_N^{(n)})_{n\in[0,N]}$ be the functions defined above. The following asymptotic formulas hold:*

$$\begin{aligned} \forall x \in \partial C, \qquad & \Psi_\epsilon(x) = \sum_{n=1}^{N} \epsilon^n \Psi_N^{(n)} + o(\epsilon^N), \\ \forall x \in \partial\Omega, \qquad & u_\epsilon(x) - u(x) = \sum_{n=1}^{N} \epsilon^n (I+\mathcal{E})^{-1}[v_n^N](x) + o(\epsilon^N). \end{aligned}$$

The remainder $o(\epsilon^N)$ depends only on N, R and $||h||_{\mathcal{C}^2}$.

We can now compute the first order term in the expansion of $\widetilde{c_{\text{flr}}}$.

Recall that $\widetilde{c_{\text{flr}}} = \delta\,[u_\epsilon]\big|_{\partial C_\epsilon}$. The boundary conditions (8.4), that u_ϵ satisfies, give us

$$\widetilde{c_{\text{flr}}} = \delta\beta\frac{\partial u_\epsilon}{\partial\nu} = -\delta\Psi_\epsilon.$$

Let us find the first order approximation of Ψ_ϵ. We apply the previous procedure to obtain $\Psi_1^{(1)}$. Hence, one introduces:

$$\begin{aligned} \Psi_0^{(0)} &= -\beta(I+\beta\mathcal{L})^{-1}\left[\frac{\partial H}{\partial\nu}\right], \\ \Psi_0^{(1)} &= -\beta(I+\beta\mathcal{L})^{-1}\left[-\frac{h'}{R^2}\frac{\partial H}{\partial\theta} + h\frac{\partial^2 H}{\partial r^2} - h\frac{\partial}{\partial r}\mathcal{D}_C^{(0)}(\Psi_0^{(0)})\right]. \end{aligned} \tag{10.35}$$

Observe that $\Psi_0^{(0)} = \Psi$. Thanks to (10.34), one can write v_1^0 for all $x\in\partial\Omega$:

$$v_1^0(x) = -\frac{1}{R}\int_0^{2\pi}\frac{\partial}{\partial\theta^y}\left(h(\theta^y)\frac{\partial}{\partial\theta^y}\Gamma^{(0)}(x,y)\right)\Psi(\theta^y)d\theta^y + \mathcal{D}_C^{(0)}[\Psi_0^{(1)}](x). \tag{10.36}$$

Therefore, we get

$$\begin{aligned} \Psi_1^{(0)} &= \Psi_0^{(0)} = \Psi \\ \Psi_1^{(1)} &= -\beta(I+\beta\mathcal{L})^{-1}\left(-\frac{h'}{R^2}\frac{\partial H}{\partial\theta} + h\frac{\partial^2 H}{\partial r^2} + \frac{\partial}{\partial r}\mathcal{D}_\Omega^{(0)}\,(I+\mathcal{E})^{-1}[v_1^0] - h\frac{\partial}{\partial r}\mathcal{D}_C^{(0)}[\Psi]\right). \end{aligned} \tag{10.37}$$

We first recall the mapping properties of the operators $\mathcal{K}_D^{(0)}$ and $(\mathcal{K}_D^{(0)})^*$. It is known that if D is a $\mathcal{C}^{2,\eta}$ domain, then $\mathcal{K}_D^{(0)}$ and $(\mathcal{K}_D^{(0)})^*$ map continuously $\mathcal{C}^{1,\eta}(\partial D)$ into $\mathcal{C}^{2,\eta}(\partial D)$ (see, for instance, [127]). We also need the following result.

Lemma 10.2.2. *Let D be a $\mathcal{C}^{2,\eta}$ domain in $\mathbb{R}^2$, for $0<\eta<1$. Let $\Psi\in\mathcal{C}^{1,\eta}(\partial D)$. We have*

$$\frac{\partial}{\partial T}\mathcal{D}_D^{(0)}[\Psi]\bigg|_{\pm} = \mp\frac{1}{2}\frac{\partial\Psi}{\partial T} + \frac{\partial}{\partial T}\mathcal{K}_D^{(0)}[\Psi].$$

Proof. Let $\Psi \in \mathcal{C}^{1,\eta}(\partial D)$. Recall the jump relation of the double layer potential across the boundary ∂D:

$$\mathcal{D}_D^{(0)}[\Psi]|_{\pm} = \left(\mp\frac{I}{2} + \mathcal{K}_D^{(0)}\right)[\Psi].$$

The result of the proposition is simply obtained by taking the tangential derivative of the previous formula and making use of the mapping properties of $\mathcal{K}_D^{(0)}$. □

Corollary 10.2.1. *Let D be a $\mathcal{C}^{2,\eta}$ domain in $\mathbb{R}^2$, for $0 < \eta < 1$. Let $h \in \mathcal{C}^2(\partial D)$ and let $\Psi \in \mathcal{C}^{2,\eta}(\partial D)$. We have*

$$-\frac{\partial}{\partial T}h\frac{\partial}{\partial T}\mathcal{D}_D^{(0)}[\Psi]\Big|_- + \left(-\frac{I}{2} + (\mathcal{K}_D^{(0)})^*\right)\Big[-\frac{\partial}{\partial T}h\frac{\partial \Psi}{\partial T}\Big] = \frac{\partial}{\partial T}\mathcal{K}_D^{(0)}[h\frac{\partial \Psi}{\partial T}] - \frac{\partial}{\partial T}h\frac{\partial}{\partial T}\mathcal{K}_D^{(0)}[\Psi]. \tag{10.38}$$

In the particular case of the disk C, we obtain that

$$-\frac{1}{R^2}\frac{\partial}{\partial \theta}h\frac{\partial}{\partial \theta}\mathcal{D}_C^{(0)}[\Psi]\Big|_- + \left(-\frac{I}{2} + (\mathcal{K}_C^{(0)})^*\right)\Big[-\frac{1}{R^2}\frac{\partial}{\partial \theta}h\frac{\partial \Psi}{\partial \theta}\Big] = 0.$$

Proof. From Lemma 10.2.2, we know that

$$-\frac{\partial}{\partial T}h\frac{\partial}{\partial T}\mathcal{D}_D^{(0)}[\Psi]\Big|_- = -\frac{1}{2}\frac{\partial}{\partial T}h\frac{\partial \Psi}{\partial T} - \frac{\partial}{\partial T}h\frac{\partial}{\partial T}\mathcal{K}_D^{(0)}[\Psi].$$

Besides, the tangential derivative of the operator $\mathcal{K}_D^{(0)}$ can be expressed as follows [81, p.144]

$$\frac{\partial}{\partial T}\mathcal{K}_D^{(0)}[\Psi] = -(\mathcal{K}_D^{(0)})^*[\frac{\partial \Psi}{\partial T}],$$

for $\Psi \in \mathcal{C}^{2,\eta}(\partial D)$. We thus obtain easily the result (10.38).

Recall that, for a disk of radius R, the operator $\mathcal{K}_C^{(0)}$ admits the explicit formula

$$\mathcal{K}_C^{(0)}[\Psi] = \frac{1}{4\pi}\int_0^{2\pi}\Psi(\phi)d\phi,$$

which does not depend on θ. Its tangential derivative is therefore zero, and we have the formula for the disk. Finally, we note that $(\mathcal{K}_C^{(0)})^* = \mathcal{K}_C^{(0)}$ and hence,

$$(\mathcal{K}_C^{(0)})^*\Big[\frac{\partial}{\partial \theta}h\frac{\partial \Psi}{\partial \theta}\Big] = 0.$$

□

The next step is to find w such that

$$(I + \mathcal{E})[w] = v_1^0. \tag{10.39}$$

From Proposition 10.2.4, it follows that there exists a unique function w solution to (10.39). The following result holds.

Proposition 10.2.6. *The solution to (10.39) verifies the following equation and boundary conditions:*

$$\begin{cases} \Delta w = 0 & \text{in } C \cup \Omega \setminus \overline{C}, \\ \left.\dfrac{\partial w}{\partial \nu}\right|_{+} - \left.\dfrac{\partial w}{\partial \nu}\right|_{-} = -\dfrac{1}{R^2}\dfrac{\partial}{\partial \theta} h \dfrac{\partial \Psi}{\partial \theta} & \text{on } \partial C, \\ w\,|_{+} - w\,|_{-} - \beta \left.\dfrac{\partial w}{\partial \nu}\right|_{-} = -\beta \left(\dfrac{h}{R}\dfrac{\partial u}{\partial r} + \dfrac{1}{R^2}\dfrac{\partial}{\partial \theta} h \left.\dfrac{\partial u}{\partial \theta}\right|_{-} \right) & \text{on } \partial C, \\ \left.\dfrac{\partial w}{\partial \nu}\right|_{\partial \Omega} = 0 & \text{on } \partial \Omega. \end{cases} \tag{10.40}$$

Proof. The solution w of the problem (10.40) satisfies the representation formula:

$$\forall x \in \Omega, \quad w(x) = \mathcal{D}_{\Omega}^{(0)}[w|_{\partial\Omega}](x) + \mathcal{S}_{C}^{(0)}[-\frac{1}{R^2}\frac{\partial}{\partial \theta} h \frac{\partial \Psi}{\partial \theta}](x) + \mathcal{D}_{C}^{(0)}[\Lambda](x), \tag{10.41}$$

where the density Λ on ∂C is given by

$$\begin{aligned} \Lambda = -\beta(I + \beta\mathcal{L})^{-1} \Bigg[-\frac{h}{R}\frac{\partial u}{\partial r} & - \frac{1}{R^2}\frac{\partial}{\partial \theta} h \left.\frac{\partial u}{\partial \theta}\right|_{-} + \frac{\partial}{\partial \nu}\mathcal{D}_{\Omega}^{(0)}[w|_{\partial\Omega}] \\ & + \left(-\frac{I}{2} + (\mathcal{K}_C^*)^{(0)} \right) \left[-\frac{1}{R^2}\frac{\partial}{\partial \theta} h \frac{\partial \Psi}{\partial \theta} \right] \Bigg]. \end{aligned} \tag{10.42}$$

Thus, for $x \in \partial\Omega$,

$$\begin{aligned} (I + \mathcal{E})[w](x) = {} & \mathcal{S}_{C}^{(0)}[-\frac{1}{R^2}\frac{\partial}{\partial \theta} h \frac{\partial \Psi}{\partial \theta}](x) \\ & -\beta\,\mathcal{D}_{C}^{(0)}(I + \beta\mathcal{L})^{-1} \left[-\frac{h}{R}\frac{\partial u}{\partial r} - \frac{1}{R^2}\frac{\partial}{\partial \theta} h \left.\frac{\partial u}{\partial \theta}\right|_{-} + \left(-\frac{I}{2} + (\mathcal{K}_C^{(0)})^* \right) \left[-\frac{1}{R^2}\frac{\partial}{\partial \theta} h \frac{\partial \Psi}{\partial \theta} \right] \right]. \end{aligned} \tag{10.43}$$

By integrating by parts twice, the first term in our equation becomes

$$\mathcal{S}_{C}^{(0)}[-\frac{1}{R^2}\frac{\partial}{\partial \theta} h \frac{\partial \Psi}{\partial \theta}](x) = -\frac{1}{R}\int_0^{2\pi} \frac{\partial}{\partial \theta^y} \left(h(\theta^y) \frac{\partial}{\partial \theta^y} \Gamma^{(0)}(x, y) \right) \Psi(\theta^y) d\theta^y. \tag{10.44}$$

Hence, we obtain that

$$\mathcal{S}_{C}^{(0)}[-\frac{1}{R^2}\frac{\partial}{\partial \theta} h \frac{\partial \Psi}{\partial \theta}](x) = v_1^1(x) - \mathcal{D}_{C}^{(0)}[\Psi_1^{(1)}](x). \tag{10.45}$$

The representation formula of u and the expression of the Laplacian in terms of polar coordinates give us

$$\frac{1}{R^2}\frac{\partial}{\partial \theta} h \left.\frac{\partial u}{\partial \theta}\right|_{-} = \frac{h'}{R^2}\frac{\partial H}{\partial \theta} - h\frac{\partial^2 H}{\partial r^2} - \frac{h}{R}\frac{\partial H}{\partial r} + \frac{1}{R^2}\frac{\partial}{\partial \theta} h \frac{\partial}{\partial \theta} \mathcal{D}_{C}^{(0)}[\Psi] \bigg|_{-}. \tag{10.46}$$

Observe that by definition of Ψ, we have on $\partial\Omega$

$$\frac{\partial u}{\partial r} = -\beta^{-1}\Psi. \tag{10.47}$$

One can then derive the integral equation that Ψ verifies and obtain that

$$-\frac{h}{R}\frac{\partial u}{\partial r} + \frac{h}{R}\frac{\partial H}{\partial r} = -\frac{h}{R}\frac{\partial}{\partial r}\mathcal{D}_C^{(0)}[\Psi]. \tag{10.48}$$

The second term in our equation (10.43) becomes

$$-\beta\mathcal{D}_C^{(0)}(I+\beta\mathcal{L})^{-1}\left[-\frac{h'}{R^2}\frac{\partial H}{\partial\theta} + h\frac{\partial^2 H}{\partial r^2} - \frac{h}{R}\frac{\partial}{\partial r}\mathcal{D}_C^{(0)}(\Psi)\right].$$

It follows from (10.37) and (10.45) that

$$\forall x \in \partial\Omega, \qquad (I+\mathcal{E})[w](x) = v_1^0(x).$$

□

We have obtained an approximation at first order of $\widetilde{c_{\text{flr}}}$:

$$\widetilde{c_{\text{flr}}} = c_{\text{flr}} - \epsilon\delta\Psi_1^{(1)} + o(\epsilon),$$

where $\Psi_1^{(1)}$ is given by

$$\Psi_1^{(1)} = -\beta(I+\beta\mathcal{L})^{-1}\left[-\frac{h'}{R^2}\frac{\partial H}{\partial\theta} + h\frac{\partial^2 H}{\partial r^2} + \frac{\partial}{\partial r}\mathcal{D}_\Omega^{(0)}w - h\frac{\partial}{\partial r}\mathcal{D}_C^{(0)}(\Psi)\right],$$

and w is the solution of (10.40).

We can now derive the first order term in the asymptotic expansion of (10.4) as $\epsilon \to 0$.

Theorem 10.2.1. *The integral (10.4) admits the following asymptotic expansion:*

$$\begin{aligned}\int_{\partial C_\epsilon} \tilde{\gamma}\widetilde{c_{\text{flr}}}(x)\Phi_{\text{exc}}^n(x)\Phi_{\text{exc}}^m(x)ds(x) &= \int_{\partial C} \tilde{\gamma}c_{\text{flr}}(x)\Phi_{\text{exc}}^n(x)\Phi_{\text{exc}}^m(x)ds(x)\\ &+\epsilon\int_{\partial C}\tilde{\gamma}\left(A\,c_{\text{flr}}(\theta)\,h(\theta) - \delta\,B\,\Psi_1^{(1)}(\theta)\right)e^{-i(n+m)\theta}\,d\theta + o(\epsilon),\end{aligned} \tag{10.49}$$

where the constants A and B are given by

$$\begin{aligned}A &= ikJ_n'(ikR)J_m(ikR)\,R + ikJ_n(ikR)J_m'(ikR)\,R + J_n(ikR)J_m(ikR),\\ B &= J_n(ikR)J_m(ikR)\,R.\end{aligned} \tag{10.50}$$

10.2.2 Fourier coefficients of $\Psi_1^{(1)}$

Recall that Ω is the unit disk and C is the disk with radius $R < 1$. In terms of polar coordinates, the fundamental solution $\Gamma^{(0)}$ of Δ in $\mathbb{R}^2$, given by (9.9), has the expression

$$\forall y\,(r,\theta) \in \overline{\Omega},\ \forall z\,(R,\phi) \in \overline{\Omega}, \qquad \Gamma_z^0(y) = \frac{1}{4\pi}\log(R^2 + r^2 - 2rR\cos(\theta - \phi)).$$

The decomposition of log into a power series gives us the following formulas:

$$\Gamma_z^0(y) = \begin{cases} \dfrac{1}{2\pi}\log R - \dfrac{1}{4\pi}\displaystyle\sum_{n\in\mathbb{Z}^*}\frac{1}{|n|}(\frac{r}{R})^{|n|}\, e^{in(\theta-\phi)} & \text{if } r < R, \\ \dfrac{1}{2\pi}\log r - \dfrac{1}{4\pi}\displaystyle\sum_{n\in\mathbb{Z}^*}\frac{1}{|n|}(\frac{R}{r})^{|n|}\, e^{in(\theta-\phi)} & \text{if } R < r, \end{cases} \tag{10.51}$$

where $\mathbb{Z}^* = \mathbb{Z} \setminus \{0\}$. Let $f \in L^2(]0, 2\pi[)$. By reinjecting (10.51) into the definition of the following operators, we obtain for $y(R,\theta) \in \partial C$ that

$$\begin{aligned} \mathcal{S}_\Omega^{(0)}[f](y) &= -\frac{1}{2}\sum_{n\in\mathbb{Z}^*}\frac{1}{|n|}R^{|n|}\,\hat{f}(n)\,e^{in\theta}, \\ \mathcal{D}_\Omega^{(0)}[f](y) &= \hat{f}(0) + \frac{1}{2}\sum_{n\in\mathbb{Z}^*}R^{|n|}\,\hat{f}(n)\,e^{in\theta}, \\ \frac{\partial\mathcal{D}_\Omega^{(0)}}{\partial r}[f](y) &= \frac{1}{2}\sum_{n\in\mathbb{Z}^*}|n|R^{|n|-1}\,\hat{f}(n)\,e^{in\theta}, \\ \frac{\partial\mathcal{D}_C^{(0)}}{\partial r}[f](y) &= \frac{1}{2}\sum_{n\in\mathbb{Z}^*}|n|\,\frac{1}{R}\,\hat{f}(n)\,e^{in\theta}. \end{aligned}$$

Recall that H satisfies the following representation formula on ∂C:

$$H = -\mathcal{S}_\Omega^{(0)}[g_{\text{ele}}] + \mathcal{D}_\Omega^{(0)}[f_0],$$

where $g_{\text{ele}} = \left.\dfrac{\partial u}{\partial \nu}\right|_{\partial\Omega}$ and $f_0 = u|_{\partial\Omega}$. We therefore get

$$\begin{aligned} H(\theta) &= \hat{f}_0(0) + \frac{1}{2}\sum_{n\in\mathbb{Z}^*}\left(\frac{1}{|n|}\hat{g}_{\text{ele}}(n) + \hat{f}_0(n)\right)R^{|n|}\,e^{in\theta}, \\ \frac{\partial H}{\partial \theta}(\theta) &= \sum_{n\in\mathbb{Z}^*} in\,\widehat{H}(n)\,e^{in\theta}, \\ \frac{\partial^2 H}{\partial r^2}(\theta) &= \frac{1}{R^2}\sum_{n\in\mathbb{Z}^*}|n|(|n|-1)\widehat{H}(n)\,e^{in\theta}. \end{aligned}$$

Besides, for $f \in \mathcal{C}^{2,\eta}(\partial C)$, we have

$$(I+\beta\mathcal{L})^{-1}[f](\theta) = \sum_{n\in\mathbb{Z}^*} \left(1+\beta\frac{|n|}{2R}\right)^{-1} \hat{f}(n)\, e^{in\theta}.$$

Note that $\widehat{\Psi}(n) = -\beta\left(1+\beta\frac{|n|}{2R}\right)^{-1}\frac{|n|}{R}\,\widehat{H}(n)$.

We can now write the Fourier coefficients of $\Psi_1^{(1)}$, for $n \in \mathbb{Z}^* := \{m \in \mathbb{Z}, m \neq 0\}$,

$$\begin{aligned}\widehat{\Psi_1^{(1)}}(n) &= -\beta\frac{1}{2}\frac{|n|\,R^{|n|-1}}{1+\beta\dfrac{|n|}{2R}}\,\hat{w}(n) - \beta\sum_{p=-\infty}^{\infty}\hat{h}(p)\widehat{H}(n-p) \\ &\times\left((n-p)p + |n-p|(|n-p|-1) + \frac{\beta}{R}\frac{|n-p|^2}{2R+\beta\,|n-p|}\right)\left(1+\beta\frac{|n|}{2R}\right)^{-1}.\end{aligned} \tag{10.52}$$

Integral (10.4) becomes at first order:

$$\begin{aligned}\mathcal{I}_\epsilon^{m,n} = \mathcal{I}_0^{m,n} \quad &+\epsilon\, 2\pi\, A\,\delta\,\beta\tilde{\gamma}\sum_{p=-\infty}^{\infty}\hat{h}(p)\widehat{H}(m+n-p)\left(1+\beta\frac{|m+n-p|}{2R}\right)^{-1} \\ &-\epsilon\, 2\pi\, B\,\delta\,\tilde{\gamma}\,\widehat{\Psi_1^{(1)}}(m+n),\end{aligned}$$

where $\mathcal{I}_\epsilon^{m,n} = \int_{\partial C_\epsilon}\tilde{\gamma}\widetilde{c_{\text{flr}}}(x)\Phi_{\text{exc}}^n(x)\Phi_{\text{exc}}^m(x)\,ds(x)$ and $\mathcal{I}_0^{m,n} = \int_{\partial C}\tilde{\gamma}c_{\text{flr}}(x)\Phi_{\text{exc}}^n(x)\Phi_{\text{exc}}^m(x)ds(x)$.

10.2.3 Reconstruction of h

We introduce the linear operator $\mathcal{Q}$ defined on $\mathcal{C}^2(\partial C)$ by

$$(\mathcal{Q}[\hat{h}])_{m,n} = \epsilon\sum_{p=-\infty}^{\infty}F_{m,n}(p)\,\hat{h}(p),$$

where

$$\begin{aligned}F_{m,n}(p) = 2\pi\delta\beta\tilde{\gamma}\Bigg[&\frac{A}{1+\beta\dfrac{|m+n-p|}{2R}} + \frac{B}{1+\beta\dfrac{|m+n|}{2R}}\Bigg((m+n-p)p \\ &+|m+n-p|(|m+n-p|-1) + \frac{\beta}{R}\frac{|m+n-p|^2}{2R+\beta\,|m+n-p|}\Bigg)\Bigg]\widehat{H}(m+n-p).\end{aligned}$$

Recall that $\mathcal{I}_\epsilon^{m,n}$ and $\mathcal{I}_0^{m,n}$ can be computed from the knowledge of the outgoing light intensities $I_{\text{emt},\epsilon}^n$ and I_{emt}^n measured at the boundary of our domain (10.2), (10.3):

$$\mathcal{I}_\epsilon^{m,n} = 2\pi\,E_m\,\widehat{I_{\text{emt},\epsilon}^n}(m), \qquad \mathcal{I}_0^{m,n} = 2\pi\,E_m\,\widehat{I_{\text{emt}}^n}(m).$$

We denote $\hat{a}$ the data of our problem:

$$\forall m, n \in \mathbb{Z}, \qquad \hat{a}_{m,n} := 2\pi E_m\Big(\widehat{I^n_{\mathrm{emt},\epsilon}}(m) - \widehat{I^n_{\mathrm{emt}}}(m)\Big) - \epsilon\,\tilde{\gamma} B\,\beta\,\pi\,\delta\,\frac{|m+n|\,R^{|m+n|-1}}{1+\beta\dfrac{|m+n|}{2R}}\,\hat{w}(m+n),$$

where ϵw is the measured difference of the voltage potential on $\partial\Omega$, when the cell occupies C_ϵ and when it is the circle C.

The operator $\mathcal{Q}$ links the perturbation h of the membrane cell to the data of our problem:

$$\hat{a}_{m,n} = (\mathcal{Q}[\hat{h}])_{m,n} + \epsilon^2 \hat{V}_{m,n},$$

with the term $\epsilon^2 \hat{V}_{m,n}$ modeling the linearization error.

We choose to apply at the boundary of our domain Ω an electric field $g_{\mathrm{ele}} : \theta \to e^{iz\theta}$ with $z \in \mathbb{Z}$. Let us compute the resulting voltage potential at the boundary of Ω, f_0 and more specifically its Fourier coefficients. From the representation formula (9.10) of u and the jumps relation of the single and double layer potentials, we obtain the following equation at the boundary of our domain:

$$f_0 = -\mathcal{S}^{(0)}_\Omega[g_{\mathrm{ele}}] + \frac{1}{2} f_0 + \mathcal{K}^{(0)}_\Omega[f_0] + \mathcal{D}^{(0)}_C[\Psi].$$

Since $\displaystyle\int_{\partial\Omega} f_0 = 0$ from (8.4), we immediately get $\hat{f}_0(0) = 0$ and $\mathcal{K}^{(0)}_\Omega[f_0] = 0$. We write, like in the previous section, the Fourier coefficients of the various layer potentials and of Ψ and get for $n \in \mathbb{Z}^*$:

$$\hat{f}_0(n) = \frac{2(1+\beta\dfrac{|n|}{2R}) + \beta|n|R^{2|n|-2}}{2(1+\beta\dfrac{|n|}{2R}) - \beta|n|R^{2|n|-2}}\,\frac{1}{|n|}\,\hat{g}_{\mathrm{ele}}(n).$$

Note that $\hat{g}_{\mathrm{ele}}(n) = \delta_z(n)$. We can now write the Fourier coefficients of $H|_{\partial C}$ in our case:

$$\widehat{H}(0) = 0, \qquad \text{and} \qquad \forall n \in \mathbb{Z}^*,\ \widehat{H}(n) = \frac{2(1+\beta\dfrac{|n|}{2R})}{2(1+\beta\dfrac{|n|}{2R}) - \beta|n|R^{2|n|-2}}\,\frac{1}{|n|}\,\delta_z(n) R^{|z|}.$$

The operator $\mathcal{Q}$ has therefore the following simplified expression:

$$(\mathcal{Q}[\hat{h}])_{m,n} = \epsilon\, F_{m,n}(z)\,\hat{h}(m+n-z),$$

where

$$F_{m,n}(z) = \left[\frac{A}{1+\beta\dfrac{|z|}{2R}} + \frac{B}{1+\beta\dfrac{|m+n|}{2R}}\left((m+n-z)z + |z|(|z|-1) + \frac{\beta}{R}\frac{|z|^2}{2R+\beta\,|z|}\right)\right]$$
$$\times \frac{2\pi\delta\beta\tilde{\gamma}}{|z|}\,\frac{2(1+\beta\dfrac{|z|}{2R})}{2(1+\beta\dfrac{|z|}{2R}) - \beta|z|R^{2|z|-2}}\,R^{|z|}.$$

Recall that the constants A and B depend on R and k.

The adjoint of the operator $\mathcal{Q}$ is given by

$$(\mathcal{Q}^{\star}[\hat{a}])_p = \epsilon \sum_{j=-\infty}^{\infty} \overline{F}_{j,p+z-j}(z)\, \hat{a}_{j,p+z-j}.$$

Then we obtain that

$$(\mathcal{Q}^{\star}\mathcal{Q}[\hat{h}])_p = \epsilon^2 \sum_{j=-\infty}^{\infty} |F_{j,p+z-j}(z)|^2\, \hat{h}(p).$$

We now consider the presence of measurement or instrument noise in our measured data. We thus introduce

$$\hat{a}^{meas}_{m,n} = (\mathcal{Q}[\hat{h}])_{m,n} + \epsilon^2 \hat{V}_{m,n} + \sigma \hat{W}_{m,n},$$

with the noise term $\hat{W}_{m,n}$ modeled as independent standard complex circularly symmetric Gaussian random variables (such that $\mathbb{E}[|\hat{W}_{m,n}|^2] = 1$; $\mathbb{E}$ being the expectation). Here, σ corresponds to the noise magnitude. We consider that σ verifies $\epsilon^2 \ll \sigma$, so that the linearization error is negligible over the measurement error and we can write:

$$\hat{a}^{meas}_{m,n} = (\mathcal{Q}[\hat{h}])_{m,n} + \sigma \hat{W}_{m,n}.$$

Following the methodology of [20, 24], we want to asses the resolving power of the measured data in the presence of this noise.

Since h is $\mathcal{C}^2$, $|\hat{h}(p)| \leq C/p^2$ for some constant C, for all $p \in \mathbb{Z}^*$. Besides, one can see that for all $m, n \in \mathbb{Z}$, $F_{m,n}$ is bounded, for given R and k. Let M be a positive real such that $M \ll 1/\epsilon^2$. We can reconstruct the Fourier coefficients of the shape deformation h only for p such that $|p| \leq M$, otherwise the linearization error $\epsilon^2 \hat{V}_{m,n}$ is too large. We suppose that $\hat{h}_p = 0$ for all $|p| \geq M$.

To reconstruct h, one can minimize the following quadratic functional over φ:

$$\left|\left| \mathcal{Q}[\hat{\varphi}] - \hat{a}^{meas} \right|\right|^2_F,$$

where $\hat{a}^{meas} = (\hat{a}^{meas}_{m,n})_{m,n}$, $\hat{\varphi} = (\hat{\varphi}(p))_p$, and $||\ ||_F$ is the Frobenius norm. The obtained least squares estimate is given by

$$\forall p \in [-M, M], \quad \hat{h}_{est}(p) = (\mathcal{Q}^{\star}\mathcal{Q})^{-1}\mathcal{Q}^{\star}[\hat{a}^{meas}](p) = \hat{h}(p) + \sigma\left((\mathcal{Q}^{\star}\mathcal{Q})^{-1}\mathcal{Q}^{\star}[\hat{W}]\right)_p. \tag{10.53}$$

One can prove with the explicit formulas of the operators $\mathcal{Q}$ and $\mathcal{Q}^{\star}$ that the following result holds.

Proposition 10.2.7. *Estimation (10.53) is unbiased and has the following variance:*

$$\mathbb{E}\left(|\hat{h}_{est}(p) - \hat{h}(p)|^2\right) = \frac{\sigma^2}{\epsilon^2}\left(\sum_{j=-\infty}^{\infty} |F_{j,p+z-j}|^2\right)^{-1}. \tag{10.54}$$

Besides Proposition 10.2.7, Parseval's identity and Graf's addition formula yield

$$\sum_{j=-\infty}^{\infty} |F_{j,p+z-j}|^2 = \frac{2}{\pi} \int_0^{\pi/2} |f_p(\theta)|^2 d\theta,$$

where the function f_p is defined by

$$f_p(\theta) = a\, 2ikR \sin(\theta)\, J'_{p+z}(2ikR\sin(\theta)) + (a + Rb)\, J_{p+z}(2ikR\sin(\theta)),$$

$$\text{with} \quad a(R,z) = \frac{2R^{|z|}}{2(1+\beta\frac{|z|}{2R}) - \beta|z|R^{2|z|-2}} \frac{2\pi\delta\beta\tilde{\gamma}}{|z|},$$

$$b(R,p,z) = a(R,z)\,\frac{2R+\beta\,|p+z|}{2R+\beta\,|z|}\left(pz + |z|(|z|-1) + \frac{\beta}{R}\frac{|z|^2}{2R+\beta\,|z|}\right).$$

We introduce the signal to noise ratio SNR:

$$\text{SNR} = (\frac{\epsilon}{\sigma})^2. \tag{10.55}$$

The following result holds thanks to (10.54).

Theorem 10.2.2. *Suppose that the pth mode of h, $\hat{h}(p)$, is of order 1, we can resolve it if the following condition is satisfied:*

$$SNR^{-1} < \frac{2}{\pi} \int_0^{\pi/2} |f_p(\theta)|^2 d\theta.$$

Let us simplify this stability condition under the respective asymptotic assumptions $|k|R \gg 1$ and $|k|R \ll 1$.

Since $J_{-n} = (-1)^n J_n$ ([2, Formula 9.1.5]), we can consider without any restriction that $p + z \geq 0$.

Assumption 1: $|\mathbf{k}|\mathbf{R} \gg \mathbf{1}$ We assume in this paragraph that $|k|R \gg 1$. We use the asymptotic expansions of the Bessel functions of the first kind and their derivative ([2, Formulas 9.2.5 and 9.2.11]) to find that, in this case, when $p + z < 2|k|R$, we have

$$\frac{2}{\pi} \int_0^{\pi/2} |f_p(\theta)|^2 d\theta \sim \frac{4a^2}{\pi^2} |k| R \sum_{n=0}^{\infty} \frac{(4Im(ik)R)^{2n}}{(2n)!} \frac{2^{2n}(n!)^2}{(2n+1)!}.$$

Then the resolving condition becomes

$$\text{SNR}^{-1} < C(R,z)|k| \qquad \text{with} \quad C(R,z) = \frac{4\,a(R,z)^2}{\pi^2} R \sum_{n=0}^{\infty} \frac{(4Im(ik)R)^{2n}}{(2n)!} \frac{2^{2n}(n!)^2}{(2n+1)!}.$$

With large $|k|R$, we can estimate the coefficients $\hat{h}(p)$ for all SNR of order $1/|k|$, as long as $p + z < 2|k|R$.

When $p + z > 2|k|R$, from [2, Formulas (9.3.35) and (9.3.43)] it follows that the following asymptotic behavior of our integrand holds:

$$|f_p(\theta)|^2 \sim \frac{\sqrt{|1-x|}}{2(p+z)\pi} \left|1+\sqrt{1-x}\right|^{-(p+z)} e^{2(p+z)Re(\sqrt{1-x})}\, x^{2(p+z-1)},$$

where $x = \left(\frac{2ikR\sin(\theta)}{p+z}\right)^2$.

Since $|x| < 1$, the last term in the preceding expression is the dominant one, and makes the integral exponentially small. To resolve the pth mode of h in this context, we therefore need a SNR exponentially large, which is impossible in practice.

We choose for each $p < M$ an electric model with $z < 2|k|R - p$. The condition $p + z < 2|k|R$ is in this way always satisfied, and the pth mode can be resolved as long as $\mathrm{SNR}^{-1} < C(R, z)|k|$.

For a fixed z, k and SNR, this inequality gives us a constraint on the cell radius. In order to be able to image the cell with a given SNR, its radius has to be larger than a minimal value, $R^\star$ given by

$$R^\star(\mathrm{SNR}) = \mathcal{F}^{-1}(\mathrm{SNR}^{-1}),$$

with

$$\mathcal{F}(t) = \frac{4\,a(t,z)^2}{\pi^2} t|k| \sum_{n=0}^{\infty} \frac{(4\,Re(k)t)^{2n}}{(2n)!} \frac{2^{2n}(n!)^2}{(2n+1)!}.$$

The typical size of eukaryotes cell is $10/100\,\mu$m. We use for our different parameters the following realistic values reported in [54], [50], [56], [68]:

- the absorption coefficient $\mu = 0.03$,
- the reduced scattering coefficient $\mu'_s = 0.275$,
- the fluorophore quantum efficiency $\eta = 0.016$,
- the fluorophore fluorescence lifetime $\tau = 0.56\,\mathrm{s}^{-1}$,
- the fluorophore extinction coefficient $\varepsilon_{\mathrm{exc}} = 5 * 10^4\,\mathrm{mm}^{-1}\mathrm{mol}^{-1}$,
- The constant δ defined in (8.5) is given by $\delta = 0.91 * 10^{-6}\,\mathrm{mol}\,\mathrm{V}^{-1}$.

It is worth mentioning that the absorption coefficient μ is low compared to the reduced scattering coefficient μ'_s. Recall that $k = \left(\frac{\mu + i\omega/c}{D}\right)^{1/2}$. Then, for given absorption and reduced scattering coefficients, Assumption 1 corresponds to frequencies ω such that $\omega \gg 10^{16}$ and therefore, are nonphysical. The minimal radius $R^\star$ increases with z, we thus choose z such that $|z| = 1$. Since $M \sim 10$ with these values of the parameters, this choice does not impose any restriction, because we have always $M - 1 < 2|k|R$.

Assumption 2: $|\mathbf{k}|\mathbf{R} \ll 1$ Note that the larger the reduced scattering coefficient is, the smaller $|k|$ is. The asymptotic expansions of the Bessel functions of the first kind and their derivative when the argument tends to zero ([2, Formula 9.1.7]), give us the asymptotic behavior of our integral in the case of a small $|k|R$:

$$\frac{2}{\pi}\int_0^{\pi/2} |f_p(\theta)|^2 d\theta \sim \left(\frac{|k|R}{2}\right)^{2(p+z)} \frac{(2(p+z))!}{(p+z)!^4} \left(a(p+z+1)+Rb\right)^2 .$$

For fixed z, k and R, the pth mode of h can be resolved under Assumption 2 as long as the SNR verifies:

$$\mathrm{SNR}^{-1} < \left(\frac{|k|R}{2}\right)^{2(p+z)} \frac{(2(p+z))!}{(p+z)!^4} \left(a(R,z)(p+z+1)+Rb(R,p,z)\right)^2 .$$

If we consider now that the SNR, k and z are given, we can define, for each mode p, the minimal resolving radius $R^\star$, *i.e.*, the smallest radius that the cell can have if we want to resolve the pth mode of its membrane deformation.

Theorem 10.2.3. *The minimal resolving radius $R^\star$ has the following expression:*

$$R^\star(SNR, p) = \mathcal{F}_p^{-1}(SNR^{-1}),$$

where the function $\mathcal{F}_p$ in this regime is given by

$$\mathcal{F}_p(t) = \left(\frac{|k|t}{2}\right)^{2(p+z)} \frac{(2(p+z))!}{(p+z)!^4} \left(a(t,z)\,(p+z+1)+t\,b(t,p,z)\right)^2 .$$

Note that the higher the reduced scattering coefficient is, the better the resolving power of the imaging method is. In fact, in order to resolve the mode p, the higher the reduced scattering coefficient is, the smaller the required SNR is.

We plot in Figure 10.1 this minimal resolving radius as a function of the SNR for $p = 0$, 1, 2 and 3. We centered the y-axis on the typical radii of eukaryotes cells, like in the preceding paragraph. Assumption 2 corresponds to frequencies ω such that $\omega \ll 10^{13}$. We choose $\omega = 10^9$, which is a typical frequency used in cellular tomography. For each p, we took $z = \delta_0(p) - p$, because $R^\star$ decreases with $p+z$. Since we can not take $z = 0$, the mode 0 is not the easiest to resolve. For the other parameters, we kept the values of the previous paragraph.

Under Assumption 1, for given z, R and SNR, if the resolving condition was verified, we could resolve all modes of h up to M. Because the constraint depends this time on p, a new question arises: "how many modes can we resolve for fixed R and SNR?". We introduce the maximal mode number $p(R,\mathrm{SNR})$ defined by

$$p(R,\mathrm{SNR}) = \sup\left\{p' \in \mathbb{N}\setminus\{0\} \,|\, \inf_{1\geq p'\geq p} \mathcal{F}_{p'}(R) > \mathrm{SNR}^{-1}\right\} + \mathbb{1}_{\mathcal{F}_0(R)>\mathrm{SNR}^{-1}},$$

which answers this question.

We plot in Figure 10.2 the maximal mode number as a function of the cell radius for different values of the SNR. We took the same values of our parameters as in Figure 10.1.

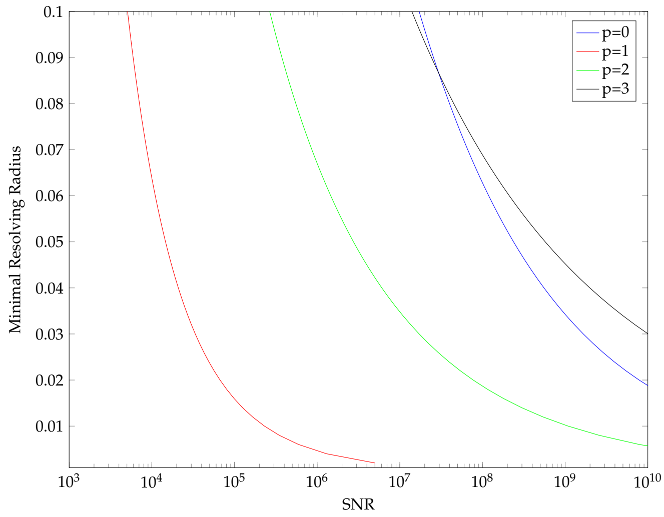

Figure 10.1: *Minimal resolving radius as function of the SNR when* $|k|R \ll 1$.

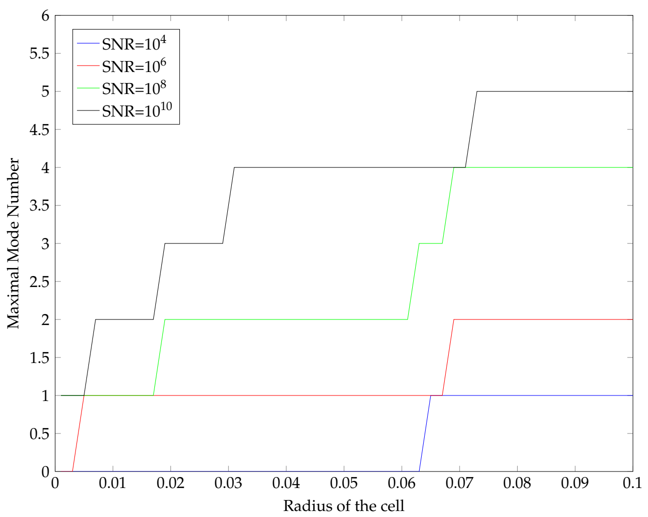

Figure 10.2: *Maximal Mode Number as function of the cell radius when* $|k|R \ll 1$.

10.3 Reconstruction of the cell membrane in the general case

We leave the specific case of a circular domain to go back to the general case in dimension two. Let $a, b \in \mathbb{R}$ with $a < b$. Let $x : [a, b] \to \mathbb{R}^2$ be a parametrization of ∂C such that $x \in \mathcal{C}^{2,\eta}(\mathbb{R})$ for an $\eta > 0$ and $|x'| = 1$. The outward unit normal to ∂C at $x(t)$, $\nu(x)$ and the tangential vector, $T(x)$, are given by

$$\nu(x) = R_{-\frac{\pi}{2}} x'(t), \qquad T(x) = x'(t),$$

where $R_{-\frac{\pi}{2}}$ is rotation by $-\frac{\pi}{2}$.

We introduce the curvature τ defined for all $x \in \partial C$ by

$$x''(t) = \tau(x)\nu(x).$$

Let C_ϵ be an ϵ-perturbation of C, *i.e.*, there is $h \in \mathcal{C}^2([a, b])$, such that ∂C_ϵ is given by

$$\partial C_\epsilon = \{\tilde{x}; \tilde{x}(t) = x(t) + \epsilon\, h(t)\nu(x(t)), t \in [a, b]\}.$$

Like in the previous section, our goal is to reconstruct the shape deformation h of our cell. Let $I^g_{\text{emt},\epsilon}$ (resp. I^g_{emt}) be the outgoing light intensities measured at the boundary of our domain when the cell occupies C_ϵ (resp. C) and the optical source g is applied at $\partial\Omega$. It follows from Proposition 10.1.1 that

$$\begin{aligned} &\int_{\partial C_\epsilon} \tilde{\gamma}\widetilde{c_{\text{flr}}}(x)\Phi^f_{\text{exc}}(x)\Phi^g_{\text{exc}}(x) ds(x) = \int_{\partial\Omega} f\, I^g_{\text{emt},\epsilon}\, ds(x), \\ \text{resp.} \quad &\int_{\partial C} \tilde{\gamma} c_{\text{flr}}(x)\Phi^f_{\text{exc}}(x)\Phi^g_{\text{exc}}(x)\, ds(x) = \int_{\partial\Omega} f\, I^g_{\text{emt}}\, ds(x), \end{aligned} \tag{10.56}$$

where $f, g \in L^2(\partial\Omega)$ and $\widetilde{c_{\text{flr}}}$ (resp. c_{flr}) is the concentration of fluorophores on the boundary of the cell ∂C_ϵ (resp. ∂C).

We introduce the voltage potential u such that $c_{\text{flr}} = \delta[u]|_{\partial C}$. We know, from Proposition 9.2.1, that u admits the following representation formula:

$$\forall x \in \Omega, \qquad u(x) \;=\; H(x) \;+\; \mathcal{D}^{(0)}_C[\Psi](x),$$

where the harmonic function H is given by

$$\forall x \in \mathbb{R}^2 \setminus \partial\Omega, \qquad H(x) \;=\; -\mathcal{S}^{(0)}_\Omega[g_{\text{ele}}](x) \;+\; \mathcal{D}^{(0)}_\Omega[u|_{\partial\Omega}](x),$$

and $\Psi \in \mathcal{C}^{2,\eta}(\partial C)$ satisfies the integral equation:

$$\Psi \;+\; \beta\frac{\partial \mathcal{D}^{(0)}_C[\Psi]}{\partial\nu} \;=\; -\beta\frac{\partial H}{\partial\nu} \qquad \text{on } \partial C.$$

We compute the first order approximation of $\widetilde{c_{\text{flr}}}$ using exactly the same method as in Subsection 10.2. Doing so, we arrive with the help of Corollary 10.2.2 at

$$\widetilde{c_{\text{flr}}} = c_{\text{flr}} - \epsilon\,\delta\,\Psi^{(1)}_1 + o(\epsilon),$$

where the function $\Psi_1^{(1)}$ is defined by

$$\Psi_1^{(1)} = -\beta(I+\beta\mathcal{L})^{-1}\bigg((-\tau h'\frac{\partial H}{\partial T} + h\frac{\partial^2 H}{\partial \nu^2} + \frac{\partial}{\partial \nu}\mathcal{D}_\Omega^{(0)}[w] - h\frac{\partial}{\partial \nu}\mathcal{D}_C^{(0)}[\Psi] + \frac{\partial}{\partial T}\mathcal{K}_C^{(0)}[h\frac{\partial \Psi}{\partial T}] - \frac{\partial}{\partial T}h\frac{\partial}{\partial T}\mathcal{K}_C^{(0)}[\Psi]\bigg),$$

and w is the solution to the problem

$$\begin{cases} \Delta w = 0 & \text{in } C \cup \Omega \setminus \overline{C}, \\ \dfrac{\partial w}{\partial \nu}\bigg|_+ - \dfrac{\partial w}{\partial \nu}\bigg|_- = -\dfrac{\partial}{\partial T}h\dfrac{\partial \Psi}{\partial T} & \text{on } \partial C, \\ w\,|_+ - w\,|_- - \beta\dfrac{\partial w}{\partial \nu}\bigg|_- = -\beta\left(\tau h\dfrac{\partial u}{\partial \nu} + \dfrac{\partial}{\partial T}h\dfrac{\partial u}{\partial T}\bigg|_-\right) & \text{on } \partial C, \\ \dfrac{\partial w}{\partial \nu}\bigg|_{\partial\Omega} = 0 & \text{on } \partial\Omega. \end{cases} \tag{10.57}$$

We then obtain an expansion of (10.56) as $\epsilon \to 0$.

Proposition 10.3.1. *Integral (10.56) admits at first order in ϵ the following expansion:*

$$\begin{aligned} \int_{\partial C_\epsilon} \tilde{\gamma}\widetilde{c_{\text{flr}}}(x)\Phi_{\text{exc}}^f(x)\Phi_{\text{exc}}^g(x)\,ds(x) &= \int_{\partial C} \tilde{\gamma} c_{\text{flr}}(x)\Phi_{\text{exc}}^f(x)\Phi_{\text{exc}}^g(x)\,ds(x) \\ &+ \epsilon \int_a^b \tilde{\gamma}\left(A(t)\,c_{\text{flr}}(t)\,h(t) - \delta\,B(t)\,\Psi_1^{(1)}(t)\right)dt + o(\epsilon), \end{aligned} \tag{10.58}$$

where the functions A and B are given by

$$\begin{aligned} A &= \frac{d\Phi_{\text{exc}}^f(t)}{dt}\Phi_{\text{exc}}^g(t) + \Phi_{\text{exc}}^f(t)\frac{d\Phi_{\text{exc}}^g(t)}{dt} - \tau(t)\Phi_{\text{exc}}^f(t)\Phi_{\text{exc}}^g(t), \\ B &= \Phi_{\text{exc}}^f(t)\Phi_{\text{exc}}^g(t). \end{aligned} \tag{10.59}$$

Let $f_1,\ldots,f_L$, be a finite number of linearly independent functions in $L^2(\partial\Omega)$. We introduce the functional $\mathcal{J}$ defined on $\mathcal{C}^2([a,b])$ by

$$\mathcal{J}(h) = \sum_{i,j=1}^{L}\left|\int_{\partial\Omega} f_i(I_{\text{emt},\epsilon}^{f_j} - I_{\text{emt}}^{f_j})\,ds - \epsilon\int_a^b \tilde{\gamma}\left(A_{i,j}(t)\,c_{\text{flr}}(t)\,h(t) - \delta\,B_{i,j}(t)\,\Psi_1^{(1)}(t)\right)dt\right|^2,$$

where the functions $A_{i,j}$ and $B_{i,j}$ are given by

$$\begin{aligned} A_{i,j} &= \frac{d\Phi_{\text{exc}}^{f_i}(t)}{dt}\Phi_{\text{exc}}^{f_j}(t) + \Phi_{\text{exc}}^{f_i}(t)\frac{d\Phi_{\text{exc}}^{f_j}(t)}{dt} - \tau(t)\Phi_{\text{exc}}^{f_i}(t)\Phi_{\text{exc}}^{f_j}(t), \\ B_{i,j} &= \Phi_{\text{exc}}^{f_i}(t)\Phi_{\text{exc}}^{f_j}(t). \end{aligned}$$

We reconstruct the shape deformation h by minimizing the functional $\mathcal{J}$ over h. In order to maximize the resolution of the reconstructed images, we choose $f_1, \ldots, f_L$, such that the functions $A_{i,j}$ and $B_{i,j}$ for $i, j \in [1, L]$ are highly oscillating. We will then be able to obtain a resolved reconstruction of the boundary changes h.

We introduce the operator $\Lambda : L^2(\partial\Omega) \to L^2(\partial C)$ defined by

$$\forall f \in L^2(\partial\Omega), \forall z \in \partial C, \qquad \Lambda[f](z) = \Phi^f_{\mathrm{exc}}|_{\partial C}(z) = \int_{\partial\Omega} G_z(y) f(y)\, ds(y).$$

The adjoint operator $\Lambda^\star : L^2(\partial C) \to L^2(\partial\Omega)$ is given by

$$\forall q \in L^2(\partial C), \forall y \in \partial\Omega, \qquad \Lambda^\star[q](y) = p|_{\partial\Omega}(y) = \int_{\partial C} \overline{G_z(y)}\, q(z)\, ds(z),$$

where p is the solution to the problem:

$$\begin{cases} -\Delta p + k^2 p = 0 & \text{in} \quad \Omega, \\ \left.\dfrac{\partial p}{\partial \nu}\right|_+ - \left.\dfrac{\partial p}{\partial \nu}\right|_- = -q & \text{on} \quad \partial C, \\ p|_+ - p|_- = 0 & \text{on} \quad \partial C, \\ \ell \dfrac{\partial p}{\partial \nu} + p = 0 & \text{on} \quad \partial\Omega. \end{cases} \tag{10.60}$$

We therefore obtain the following expression for $\Lambda^\star\Lambda$:

$$\forall f \in L^2(\partial\Omega), \forall y \in \partial\Omega, \qquad \Lambda^\star\Lambda[f](y) = \int_{\partial\Omega} dt f(t) \int_{\partial C} \overline{G_z(y)} G_z(t)\, ds(z).$$

Following [12, 21], we choose $f_1, \ldots, f_L$, to be the first singular vectors of the operator Λ. The number L, which fixes the resolving power of the approach, is chosen to maximize the trade-off between resolution and stability. To gain resolution, one has to choose L as large as possible. But if it is too large, then it follows from the fact that f_i is highly oscillating for large i that the algorithm is unstable in the case of noisy data [21, 19].

Concluding remarks

In this thesis we have introduced a new mathematical framework for cell membrane imaging. We have for the first time analytically exhibited the fundamental mechanisms underlying the fact that effective biological tissue electrical properties and their frequency dependence reflect the tissue composition and physiology. We have explained how the dependence of the effective electrical admittivity measures the complexity of the cellular organization of the tissue and developed electrical tissue property imaging approaches from micro-electrical data in order to improve differentiation of tissue pathologies.

In Part I, we have derived new formulas for the effective admittivity of suspensions of cells and characterized their dependance with respect to the frequency in terms of membrane polarization tensors. We have applied the formulas in the dilute case to image suspensions of cells from electrical boundary measurements. We have presented numerical results to illustrate the use of the Debye relaxation time in classifying microstructures. We also developed a selective spectroscopic imaging approach. We have shown that specifying the pulse shape in terms of the relaxation times of the dilute suspensions gives rise to selective imaging.

An important problem is to derive effective electrical properties of of dense periodic arrangements of cells such as skin cells. Another challenging problem is to extend our results to elasticity models of the cell. In [30, 25], formulas for the effective shear modulus and effective viscosity of dilute suspensions of elastic inclusions were derived. On the other hand, it was observed experimentally that the dependance of the viscosity of a biological tissue with respect to the frequency characterizes the microstructure [37, 51]. A mathematical justification and modeling for this important finding are one of our future research directions.

In Part II, we have proposed for the first time an optimal control algorithm for admittivity imaging from multi-frequency micro-electrical data. We have proved its convergence and its local stability. Our approach in Part II can be extended to elastography and can be used to image both shear modulus and viscosity tissue properties from internal displacement measurements. Another interesting problem is to image tissues with anisotropic impedance distribution from micro-electrical data.

In Part III, we have introduced and analyzed a mathematical model for optical imaging of cell membrane potentials changes induced by applied currents. We have presented a direct imaging algorithm in the linearized case and provided explicit formulas for its resolving power of the measurements in the presence of measurement noise. We have suggested an iterative algorithm for complex shapes. It would be interesting to consider the case of cluttered cells. Another challenging problem is the tracking of membrane changes in cell mechanisms such as cell division.

Our results in this thesis have potential applicability in cancer imaging, cell culturing and differentiation, food sciences and biotechnology [93, 89], and applied and environmental geophysics. They can be used to model and improve the MarginProbe system for breast cancer [135], which emits an electric field and senses the returning signal from tissue under evaluation. The greater vascularization, differently polarized cell membranes, and other anatomical differences of tumors compared with healthy tissue cause them to show different electromagnetic signatures. The ability of the probe to detect signals characteristic of cancer helps surgeons ensure the removal of all unwanted tissue around tumor margins.

Another commercial medical system to which our results can be applied is ZedScan [136]. ZedScan is based on electrical impedance spectroscopy for detecting neoplasias in cervical disease [1, 45]. Malignant white blood cells can be also detected using induced membrane polarization [112]. In food quality inspection, spectroscopic conductivity imaging can be used to detect bacterial cells [33, 133]. In applied and environmental geophysics, induced membrane polarization can be used to probe up to subsurface depths of thousands of meters [126, 134].

It would be very interesting to develop a physics-based learning approach, based on Debye relaxation times, for classifying tissue organizations at the cell scale from macroscopic spectroscopic admittivity measurements. One can learn from training examples such as biopsies the underlying microstructures and then, classify unseen ones from spectroscopic measurements of their admittivities. It is challenging to construct a distance between spectroscopic measurements which allows to statistically classify or separate different microstructures into different groups.

Appendix A

Extension lemmas, norm equivalence, and existence result

A.1 Extension lemmas

Due to the problem settings of this chapter, we need to study convergence properties of functions that are defined on the multiple connected sets $\mathbb{R}_2^+$, $\Phi(\mathbb{R}_2^+)$ and $\varepsilon\Phi(\mathbb{R}_2^-)$. Extension operators becomes useful to treat such functions.

Consider two open sets $U, V \subset \mathbb{R}^2$ with the relation $U \subset V$, and two Sobolev spaces $W^{1,p}(U)$ and $W^{1,p}(V)$, $p \in [1,\infty]$. What we call an *extension operator* is a bounded linear map $P : W^{1,p}(U) \to W^{1,p}(V)$, such that $Pu = u$ a.e. on U for all $u \in W^{1,p}(U)$. In this section, we introduce several extension operators of this kind that are needed in the chapter. They extend functions that are defined on Y^-, $\mathbb{R}_2^+$, $\Phi(\mathbb{R}_2^+)$ and $\varepsilon\Phi(\mathbb{R}_2^+)$ (hence Ω_ε^+) respectively.

Throughout this section, the short hand notion $\mathcal{M}_A(f)$ for a measurable set $A \subset \mathbb{R}^2$ with positive volume and a function $f \in L^1(A)$ denotes the mean value of f in A, that is

$$\mathcal{M}_A(f) = \frac{1}{|A|}\int_A f(x)dx. \tag{A.1}$$

We start with an extension operator inside the unit cube Y. Since Y^- has smooth boundary, there exists an extension operator $S : W^{1,p}(Y^+) \to W^{1,p}(Y)$ such that for all $f \in W^{1,p}(Y^+)$ and $p \in [1,\infty)$,

$$\|Sf\|_{L^p(Y)} \leq C\|f\|_{L^p(Y^+)}, \quad \|Sf\|_{W^{1,p}(Y)} \leq C\|f\|_{W^{1,p}(Y^+)}, \tag{A.2}$$

where C only depends on p and Y^-. Such an S is given in [57, section 5.4], where the second estimate above is given; the first estimate easily follows from their construction as well. Cioranescu and Saint Paulin [48] constructed another extension operator which refines the second estimate above. For the reader's convenience, we state and prove their result in the following. Similar results can be found in [73] as well.

Theorem A.1.1. *Let Y, Y^+ and Y^- be as defined in section 1.1; in particular, ∂Y^- is smooth. Then there exists an extension operator $P : W^{1,p}(Y^+) \to W^{1,p}(Y)$ satisfying that for any $f \in W^{1,p}(Y^+)$ and $p \in [1, \infty)$,*

$$\|\nabla Pf\|_{L^p(Y)} \le C\|\nabla f\|_{L^p(Y^+)}, \quad \|Pf\|_{L^p(Y)} \le C\|f\|_{L^p(Y^+)}, \tag{A.3}$$

where C only depends on the dimension and the set Y^-.

Proof. Recall the mean operator $\mathcal{M}$ in (A.1) and the extension operator S in (A.2). Given f, we define Pf by

$$Pf = \mathcal{M}_{Y^+}(f) + S(f - \mathcal{M}_{Y^+}(f)). \tag{A.4}$$

Then by setting $\psi = f - \mathcal{M}_{Y^+}(f)$, we have that

$$\|\nabla Pf\|_{L^p(Y)} = \|\nabla S\psi\|_{L^p(Y)} \le C\|\psi\|_{W^{1,p}(Y^+)} \le C\|\nabla\psi\|_{L^p(Y^+)} = C\|\nabla f\|_{L^p(Y^+)}.$$

In the second inequality above, we used the Poincaré–Wirtinger inequality for ψ and the fact that ψ is mean-zero on Y^+. The L^2 bound of Pf follows from the observation

$$\|\mathcal{M}_{Y^+}(f)\|_{L^p(Y)} \le \left(\frac{|Y|}{|Y^+|}\right)^{\frac{1}{p}} \|f\|_{L^p(Y^+)}$$

and the L^p estimate of Sf in (A.2). This completes the proof. □

Apply the extension operator on each translated cubes in $\mathbb{R}^+_2$, we get the following.

Corollary A.1.1. *Recall the definition of Y_n, Y_n^+ and Y_n^- in section 1.1. Abuse notations and define*

$$(Pu)|_{Y_n} = P(u|_{Y_n^+}), \quad n \in \mathbb{Z}^2, u \in W^{1,p}_{\mathrm{loc}}(\mathbb{R}^+_2). \tag{A.5}$$

Then P is an extension operator from $W^{1,p}_{\mathrm{loc}}(\mathbb{R}^+_2)$ to $W^{1,p}_{\mathrm{loc}}(\mathbb{R}^2)$. Further, with the same positive constant C in (A.3) *and for any $n \in \mathbb{Z}^2$, we have*

$$\|\nabla Pu\|_{L^p(Y_n)} \le C\|\nabla u\|_{L^p(Y_n^-)}, \quad \|Pu\|_{L^p(Y_n)} \le C\|u\|_{L^p(Y_n^-)}. \tag{A.6}$$

Given a diffeomorphism, the extension operator P can be transformed as follows. In the same manner, under the map of scaling, the extension operator is naturally defined.

Corollary A.1.2. *Let $\Phi(\cdot, \gamma)$ be a random diffeomorphism satisfying* (1.14) *and* (1.15). *Denote the inverse function Φ^{-1} by Ψ. Define P_γ as*

$$P_\gamma u = [P(u \circ \Phi)] \circ \Psi, \quad u \in W^{1,p}_{\mathrm{loc}}(\Phi(\mathbb{R}^+_2)). \tag{A.7}$$

Then P_γ is an extension operator from $W^{1,p}_{\mathrm{loc}}(\Phi(\mathbb{R}^+_2))$ to $W^{1,p}_{\mathrm{loc}}(\Phi(\mathbb{R}^2))$ which satisfies that

$$\|\nabla P_\gamma u\|_{L^p(\Phi(Y_n))} \le C\|\nabla u\|_{L^p(\Phi(Y_n^-))}, \quad \|P_\gamma u\|_{L^p(\Phi(Y_n))} \le C\|u\|_{L^p(\Phi(Y_n^-))}, \tag{A.8}$$

where the constant C depends further on the constants in (1.14) *and* (1.15).

Corollary A.1.3. *Let $\Phi(\cdot,\gamma)$ and Ψ be as above. For each $\varepsilon > 0$, define P^ε_γ as follows: for any $u \in W^{1,p}_{\text{loc}}(\varepsilon\Phi(\mathbb{R}^+_2))$, $P^\varepsilon_\gamma u$ is defined on each deformed and scaled cube $\varepsilon\Phi(Y_n)$ by*

$$P^\varepsilon_\gamma u(x) = \varepsilon P\tilde{u}(\Psi(\frac{x}{\varepsilon})), \tag{A.9}$$

where $\tilde{u} = \varepsilon^{-1}u \circ \varepsilon\Phi$ and P is as in (A.6). *Then P^ε_γ is an extension operator from $W^{1,p}_{\text{loc}}(\varepsilon\Phi(\mathbb{R}^+_2))$ to $W^{1,p}_{\text{loc}}(\varepsilon\Phi(\mathbb{R}^2))$ which satisfies that for any $n \in \mathbb{Z}^2$,*

$$\|\nabla P^\varepsilon_\gamma u\|_{L^p(\varepsilon\Phi(Y_n))} \le C\|\nabla u\|_{L^p(\varepsilon\Phi(Y_n^-))}, \quad \|P^\varepsilon_\gamma u\|_{L^p(\varepsilon\Phi(Y_n))} \le C\|u\|_{L^p(\varepsilon\Phi(Y_n^-))}, \tag{A.10}$$

where the constant C depends on the same parameters as stated below (A.8).

Proof. We focus on proving (A.10). Under the change of variable $x = \varepsilon\Phi(y)$, we have

$$\nabla_x P^\varepsilon_\gamma u(x) = \nabla\Psi(\frac{x}{\varepsilon})\nabla_y P\tilde{u}(\Phi^{-1}(\frac{x}{\varepsilon})) = \nabla\Psi(\Phi(y))\nabla_y P\tilde{u}(y),$$

On each deformed and scaled cube $\varepsilon\Phi(Y_n)$, we calculate

$$\begin{aligned}\|\nabla P^\varepsilon_\gamma u\|^p_{L^p(\varepsilon\Phi(Y_n))} &= \int_{\varepsilon\Phi(Y_n)} |\nabla_x P^\varepsilon_\gamma u(x)|^p dx = \int_{Y_n} |\nabla\Psi(\Phi(y))\nabla_y P\tilde{u}(y)|^p \varepsilon^2 \det(\nabla\Phi(y))dy \\ &\le \varepsilon^2 \int_{Y_n} |\nabla\Psi(\Phi(y))|^p |\nabla_y P\tilde{u}(y)|^p \det(\nabla\Phi(y))dy \le C\varepsilon^2 \int_{Y_n} |\nabla_y P\tilde{u}(y)|^p dy.\end{aligned}$$

Here, we have used the Cauchy–Schwarz inequality and the bounds (1.14)-(1.15) on the Jacobian matrix and its determinant. Upon applying (A.3), we get

$$\|\nabla P^\varepsilon_\gamma u\|^p_{L^p(\varepsilon\Phi(Y_n))} \le C\varepsilon^2 \|\nabla_y \tilde{u}\|^p_{L^p(Y_n^+)}.$$

Since $\tilde{u}(y) = \frac{1}{\varepsilon}u(\varepsilon\Phi(y))$, we have $\nabla_y\tilde{u}(y) = \nabla_y\Phi(y)\nabla_x u(\varepsilon\Phi(y))$. Change variables in the last integral and repeat the analysis above to get

$$\|\nabla_y \tilde{u}\|^p_{L^p(Y_n^+)} \le C\varepsilon^{-d}\|\nabla_x u\|^p_{L^p(\varepsilon\Phi(Y_n^+))}.$$

Combining the above estimates, one finds some C independent of ε or γ such that (A.10) holds. Moreover, the constant C is uniform for all $\varepsilon\Phi(Y_n)$. The L^2 estimate for $P^\varepsilon_\gamma u$ is simpler and ignored. This completes the proof. □

Finally, we define the extension operator from $W^{1,p}(\Omega^+_\varepsilon)$ to $W^{1,p}(\Omega)$. This is essentially the same operator in Corollary A.1.3. Indeed, recall that Ω is decomposed to the cushion K_ε and the cell containers E_ε; see (1.18). We only need to apply P^ε_γ in E_ε.

Theorem A.1.2. *Let the domains $\Omega^\pm_\varepsilon$, K_ε and E_ε be as defined in section 1.1. Let $\Phi(\cdot,\gamma)$ be a random diffeomorphism satisfying* (1.14)-(1.16). *Define the linear operator P^ε_γ as follows: for $u \in W^{1,p}(\Omega^+_\varepsilon)$, let $P^\varepsilon_\gamma u$ be given by* (A.9) *in E_ε, and let $P^\varepsilon_\gamma u = u$ in K_ε. Then P^ε_γ is an extension operator from $W^{1,p}(\Omega^+_\varepsilon)$ to $W^{1,p}(\Omega)$ and it satisfies*

$$\|\nabla P^\varepsilon_\gamma u\|_{L^p(\Omega)} \le C\|\nabla u\|_{L^p(\Omega^+_\varepsilon)}, \quad \|P^\varepsilon_\gamma u\|_{L^p(\Omega)} \le C\|u\|_{L^p(\Omega^+_\varepsilon)}, \tag{A.11}$$

where the constants C's do not depend on ε or γ.

Proof. Since P^ε_γ leaves u unchanged in K_ε and it satisfies the estimates (A.10) uniformly in the cubes $E_\varepsilon = \cup_{n\in\mathcal{I}_\varepsilon} \varepsilon\Phi(Y_n)$, we have the following:

$$\begin{aligned}\|\nabla P^\varepsilon_\gamma u\|^p_{L^p(\Omega)} &= \|\nabla u\|^p_{L^p(K_\varepsilon)} + \sum_{n\in\mathcal{I}_\varepsilon} \|\nabla P^\varepsilon_\gamma u\|^p_{L^p(\varepsilon\Phi(Y_n))} \\ &\le \|\nabla u\|^p_{L^p(K_\varepsilon)} + C\sum_{n\in\mathcal{I}_\varepsilon} \|\nabla u\|^p_{L^p(\varepsilon\Phi(Y_n^+))} \le C\|\nabla u\|^p_{L^p(\Omega_\varepsilon^+)}.\end{aligned}$$

This completes the proof of the first estimate in (A.11). The second estimate follows in the same manner, completing the proof. □

A.2 Poincaré–Wirtinger inequality

Our next goal is to derive a Poincaré–Wirtinger inequality for functions in $H^1(\Omega_\varepsilon^+)$ with a constant independent of ε and γ. The following fact of the fluctuation of a function is useful.

Lemma A.2.1. *Let $X \subset \mathbb{R}^2$ be an open bounded domain with positive volume and $f \in L^1(X)$. Assume that $X_1 \subset X$ is a subset with positive volume, then we have*

$$\|f - \mathcal{M}_{X_1}(f)\|_{L^2(X_1)} \le \|f - \mathcal{M}_X(f)\|_{L^2(X)}. \tag{A.12}$$

Proof. To simplify notations, let f_1 be the restriction of f on X_1, $m_1 = \mathcal{M}_{X_1}(f_1)$ and $\theta_1 = |X_1|/|X|$. Similarly, let f_2 be the restriction of f on $X_2 = X \setminus X_1$, $m_2 = \mathcal{M}_{X_2}(f_2)$. Let $m = \mathcal{M}_X(f)$. Then we have that

$$f - m = \begin{cases} f_1 - m_1 + (1-\theta)(m_1 - m_2), & x \in X_1, \\ f_2 - m_2 + \theta(m_2 - m_1), & x \in X_2. \end{cases}$$

Then basic computation plus the observation that $f_i - m_i$ integrates to zero on X_i for $i = 1, 2$ yield the following:

$$\|f - m\|^2_{L^2(X)} = \|f_1 - m_1\|^2_{L^2(X_1)} + \|f_2 - m_2\|^2_{L^2(X_2)} + (1-\theta)\theta|X|(m_2 - m_1)^2.$$

Since the items on the right-hand side are all non-negative, we obtain (A.12). □

Corollary A.2.1. *Assume the same conditions as in Theorem A.1.2. Then for any $u \in H^1_C(\Omega_\varepsilon^+)$, we have that*

$$\|u\|_{L^2(\Omega_\varepsilon^+)} \le C\|\nabla u\|_{L^2(\Omega_\varepsilon^+)}, \tag{A.13}$$

where the constant C does not depend on ε or γ.

Proof. Thanks to Theorem A.1.2, we extend u to $P^\varepsilon_\gamma u$ which is in $H^1(\Omega)$. Use (A.12) and the fact that $\mathcal{M}_{\Omega_\varepsilon^+}(u) = 0$ to get

$$\|u\|_{L^2(\Omega_\varepsilon^+)} \le \|P^\varepsilon_\gamma u - \mathcal{M}_\Omega(P^\varepsilon_\gamma u)\|_{L^2(\Omega)}.$$

Now apply the standard Poincaré–Wirtinger inequality for functions in $H^1(\Omega)$, and then use (A.11). We get

$$\|P^\varepsilon_\gamma u - \mathcal{M}_\Omega(P^\varepsilon_\gamma u)\|_{L^2(\Omega)} \le C\|\nabla P^\varepsilon_\gamma u\|_{L^2(\Omega)} \le C\|\nabla u\|_{L^2(\Omega_\varepsilon^+)}.$$

The constant C depends on Ω and the parameters stated in Theorem A.1.2 but not on ε or γ. The proof is now complete. □

Another corollary of the extension lemma is that we have the following uniform estimate when taking the trace of $u \in W_\varepsilon$ on the fixed boundary $\partial\Omega$.

Corollary A.2.2. *Assume the same conditions as in Theorem A.1.2. Then there exists a constant C depending on Ω and the parameters as stated in Theorem A.1.2 but independent of ε and γ such that*

$$\|u\|_{H^{\frac{1}{2}}(\partial\Omega)} \le C\|\nabla u\|_{L^2(\Omega_\varepsilon^+)}, \tag{A.14}$$

for any $u \in H^1(\Omega_\varepsilon^+)$.

Proof. Thanks to Theorem A.1.2 we extend u to $P_\gamma^\varepsilon u$ which is in $H^1(\Omega)$. The trace inequality on Ω shows

$$\|P_\gamma^\varepsilon u\|_{H^{\frac{1}{2}}(\partial\Omega)} \le C(\Omega)\|P_\gamma^\varepsilon u\|_{H^1(\Omega)}. \tag{A.15}$$

The desired estimate then follows from (A.11) and (A.13). □

A.3 Equivalence of the two norms on W_ε

In this section, we prove Proposition 1.2.2 which establishes the equivalence between the two norms on W_ε. We essentially follow [100] where the periodic case was considered. The random deformation setting requires certain modification. The details of such modifications are provided here for the reader's convenience.

The first inequality of the proposition is proved by the following lemma together with the Poincaré–Wirtinger inequality (A.13):

Lemma A.3.1. *There exists a constant C independent of ε or γ, such that*

$$\|v^\pm\|^2_{L^2(\Gamma_\varepsilon)} \le C(\varepsilon^{-1}\|v^\pm\|^2_{L^2(\Omega_\varepsilon^\pm)} + \varepsilon\|\nabla v^\pm\|^2_{L^2(\Omega_\varepsilon^\pm)}) \tag{A.16}$$

for any $v^+ \in H^1(\Omega_\varepsilon^+)$ and $v^- \in H^1(\Omega_\varepsilon^-)$.

Proof. According to the set-up, the interface Γ_ε consists of $\varepsilon\Phi(\Gamma_i)$ where $i = 1, \cdots, N(\varepsilon)$ are the labels for the deformed cubes $\{\varepsilon\Phi(Y_i)\}$ inside Ω and Γ_i are the corresponding unit scale interfaces.

Let us consider the case of $v^+ \in H^1(\Omega_\varepsilon^+)$; the other case is proved in the same manner. Denote by v_i the restriction of v^+ on the deformed cube $\varepsilon\Phi(Y_i)$. We lift this function to $\tilde{v}_i(y) = v_i(\varepsilon\Phi(y))$ which is now defined on Y_i^+. For this function, we have the trace inequality

$$\|\tilde{v}_i\|^2_{L^2(\Gamma_i)} \le C(\|\tilde{v}_i\|^2_{L^2(Y_i^+)} + \|\nabla\tilde{v}_i\|^2_{L^2(Y_i^+)}). \tag{A.17}$$

Note that this constant depends on the reference shape Y^- but is uniform in i.

On the other hand, because for any $\gamma \in \mathcal{O}$, the diffeomorphism Φ satisfies (1.14) and (1.15), the Lebesgue measures $ds(x)$ on the curve $\varepsilon\Phi(\Gamma_i)$ and $ds(y)$ on Γ_i, which are related by the change of variable $x = \varepsilon\Phi(y)$, satisfy

$$C_1 ds(x) \le \varepsilon ds(y) \le C_2 ds(x)$$

for some constant $C_{1,2}$ which depend only on the constants in the assumptions and Y^- but uniform in ε and γ.

Consequently, we have

$$\|v^+\|^2_{L^2(\Gamma_\varepsilon)} = \sum_{i=1}^{N(\varepsilon)} \int_{\varepsilon\Phi(\Gamma_i)} |v_i(x)|^2 ds(x) \le C\varepsilon \sum_{i=1}^{N(\varepsilon)} \int_{\Gamma_i} |\tilde{v}_i(y)|^2 ds(y).$$

Apply (A.17) and change the variable back; use again $dx \sim \varepsilon^2 dy$ and $\nabla_y \tilde{v}_i = \varepsilon \nabla_x v_i$ to get

$$\begin{aligned}\|v^+\|^2_{L^2(\Gamma_\varepsilon)} &\le C\varepsilon \sum_{i=1}^{N(\varepsilon)} \int_{Y_i^+} |\tilde{v}_i(y)|^2 + |\nabla_y \tilde{v}(y)|^2 dy \\ &\le C\varepsilon^{-1} \sum_{i=1}^{N(\varepsilon)} \int_{\varepsilon\Phi(Y_i^+)} |v_i(x)|^2 + \varepsilon^2 |\nabla v(x)|^2 dx\end{aligned}$$

This completes the proof of (A.16). □

The other inequality in (1.28) is implied by the following lemma:

Lemma A.3.2. *There exists a constant $C > 0$ independent of ε or γ such that*

$$\|v\|_{L^2(\Omega_\varepsilon^-)} \le C \left(\sqrt{\varepsilon} \|v\|_{L^2(\Gamma_\varepsilon)} + \varepsilon \|\nabla v\|_{L^2(\Omega_\varepsilon^-)} \right) \tag{A.18}$$

for all $v \in H^1(\Omega_\varepsilon^-)$.

Proof. We first observe that on the reference cube Y with reference cell Y^-, we have that

$$\|v\|^2_{L^2(Y^-)} \le C \left(\|v\|^2_{L^2(\Gamma_0)} + \|\nabla v\|^2_{L^2(Y^-)} \right), \tag{A.19}$$

for any $v \in H^1(Y^-)$ where C only depends on Y^- and the dimension. Indeed, suppose otherwise, we could find a sequence $\{v_n\} \subset H^1(Y^-)$ such that $\|v_n\|_{L^2(Y^-)} \equiv 1$ but

$$\|v_n\|_{L^2(\Gamma_0)} + \|\nabla v_n\|_{L^2(Y^-)} \longrightarrow 0, \quad \text{as } n \to \infty.$$

Then since $\|v_n\|_{H^1}$ is uniformly bounded, there exists a subsequence, still denoted as $\{v_n\}$, and a function $v \in H^1(Y^-)$ such that

$$v_n \rightharpoonup v \text{ weakly in } H^1(Y^-), \quad \nabla v_n \rightharpoonup \nabla v \text{ weakly in } L^2(Y^-).$$

Consequently, $\|\nabla v\|_{L^2} \le \liminf \|\nabla v_n\|_{L^2} = 0$, which implies that $v = C$ for some constant. Moreover, since the embedding $H^1(Y^-) \hookrightarrow L^2(\Gamma_0)$ is compact, the convergence $v_n \to v$ holds strongly in $L^2(\Gamma_0)$ and $\|v\|_{L^2(\Gamma)} \le \lim \|v_n\|_{L^2(\Gamma_0)} = 0$. Consequently $v \equiv 0$. On the other hand, $v_n \to v$ holds strongly in $L^2(Y^-)$ and hence $\|v\|_{L^2(Y^-)} = \lim \|v_n\|_{L^2(Y^-)} = 1$. This contradicts with the fact that $v \equiv 0$.

To prove (A.18), we lift functions in $\varepsilon\Phi(Y_i^-)$ to functions in Y_i^- as in the proof of the previous lemma, and use the scaling relations of the measures: $dx \sim \varepsilon^2 dy$ and $ds(x) \sim \varepsilon ds(y)$. We calculate

$$\|v\|^2_{L^2(\Omega_\varepsilon^-)} = \sum_{i=1}^{N(\varepsilon)} \int_{\varepsilon\Phi(Y_i^-)} |v|^2 dx \le C\varepsilon^2 \int_{Y^-} |\tilde{v}|^2 dy \le C\varepsilon^2 \sum_{i=1}^{N(\varepsilon)} \int_{\Gamma_i} |\tilde{v}|^2 ds + \int_{Y_i^-} |\nabla \tilde{v}|^2 dy$$

where in the last inequality we used (A.19). Change the variables back to get

$$\|v\|^2_{L^2(\Omega_\varepsilon^-)} \leq C\varepsilon^2 \sum_{i=1}^{N(\varepsilon)} \int_{\varepsilon\Phi(\Gamma_i)} \varepsilon^{-d+1}|v|^2 ds + \int_{\varepsilon\Phi(Y_i^-)} \varepsilon^{-d+2}|\nabla v|^2 dy.$$

Note that we used again $\nabla_y \tilde{v} = \varepsilon \nabla_x v$. The above inequality is precisely (A.18). □

Proof of Proposition 1.2.2. To prove the first inequality, we apply Lemma A.3.1 to get

$$\begin{aligned}\varepsilon\|u^+ - u^-\|^2_{L^2(\Gamma_\varepsilon)} &\leq 2(\varepsilon\|u^+\|^2_{L^2(\Gamma_\varepsilon)} + \varepsilon\|u^-\|^2_{L^2(\Gamma_\varepsilon)}) \\ &\leq C(\|u^+\|^2_{L^2(\Omega_\varepsilon^+)} + \|u^-\|^2_{L^2(\Omega_\varepsilon^-)} + \varepsilon^2\|\nabla u^+\|^2_{L^2(\Omega_\varepsilon^+)} + \varepsilon^2\|\nabla u^+\|^2_{L^2(\Omega_\varepsilon^+)}).\end{aligned}$$

Only the first term in (A.13) does not show in $\|\cdot\|_{H^1_{\mathbb{C}}\times H^1}$, but it is controlled by $\|\nabla u^+\|_{L^2(\Omega_\varepsilon^+)}$ uniformly in ε and γ thanks to (A.13).

For the second inequality, we only need to control $\|u^-\|_{L^2(\Omega_\varepsilon^-)}$. We apply Lemma A.3.2 and the triangle inequality:

$$\|u^-\|^2_{L^2(\Omega_\varepsilon^-)} \leq C\left(\varepsilon\|u^+\|^2_{L^2(\Gamma_\varepsilon)} + \varepsilon\|u^+ - u^-\|^2_{L^2(\Gamma_\varepsilon)} + \varepsilon^2\|\nabla u^-\|^2_{L^2(\Omega_\varepsilon^-)}\right).$$

Only the first term does not appear in $\|\cdot\|_{W_\varepsilon}$, but using Lemma A.3.1 and (A.13) we can bound it by

$$\varepsilon\|u^+\|^2_{L^2(\Gamma_\varepsilon)} \leq C(\|u^+\|^2_{L^2(\Omega_\varepsilon^+)} + \varepsilon^2\|\nabla u^+\|^2_{L^2(\Omega_\varepsilon^+)}) \leq C\|\nabla u^+\|^2_{L^2(\Omega_\varepsilon^+)}.$$

This completes the proof. □

A.4 Technical lemma

Lemma A.4.1. *Let φ_1 be a function in $\mathcal{D}(\Omega, C^\infty_\sharp(Y^+)) \times \mathcal{D}(\Omega, C^\infty_\sharp(Y^-))$. There exists at least one function θ in $(\mathcal{D}(\Omega, H^1_\sharp(Y^+)) \times \mathcal{D}(\Omega, H^1_\sharp(Y^-)))^2$ solution of the following problem:*

$$\begin{cases} -\nabla_y \cdot \theta^+(x,y) = 0 & \text{in } Y^+, \\ -\nabla_y \cdot \theta^-(x,y) = 0 & \text{in } Y^-, \\ \theta^+(x,y)\cdot n = \theta^-(x,y)\cdot n & \text{on } \Gamma, \\ \theta^+(x,y)\cdot n = \varphi_1^+(x,y) - \varphi_1^-(x,y) & \text{on } \Gamma, \\ y \longmapsto \theta(x,y) Y-\text{periodic}. \end{cases} \tag{A.20}$$

Proof. We look for a solution under the form $\theta = \nabla_y \eta$. We hence introduce the following variational problem:

$$\begin{cases} \text{Find } \eta \in (H^1_\sharp(Y^+)/\mathbb{C}) \times (H^1_\sharp(Y^-)/\mathbb{C}) \text{ such that} \\ \displaystyle\int_{Y^+} \nabla\eta^+(y)\cdot\overline{\psi}^+(y)dy + \int_{Y^-} \nabla\eta^-(y)\cdot\overline{\psi}^-(y)dy \\ \displaystyle\qquad\qquad = \frac{1}{\beta k_0}\int_\Gamma (\varphi_1^+ - \varphi_1^-)(\overline{\psi}^+ - \overline{\psi}^-)(y)ds(y), \\ \text{for all } \psi \in (H^1_\sharp(Y^+)/\mathbb{C}) \times (H^1_\sharp(Y^-)/\mathbb{C}), \end{cases}$$

for a fixed $x \in \Omega$. Lax-Milgram theorem gives us existence and uniqueness of such an η. Since $\varphi_1 \in \mathcal{D}(\Omega, C^\infty_\sharp(Y^+)) \times \mathcal{D}(\Omega, C^\infty_\sharp(Y^-))$, there exists at least one function $\theta \in (\mathcal{D}(\Omega, H^1_\sharp(Y^+)) \times \mathcal{D}(\Omega, H^1_\sharp(Y^-))^2$ solution of (A.20). Note that we do not have uniqueness of such a solution. $\square$

Appendix B

The convergence of the Landweber sequence with a Hilbert projection

This appendix follows from [69]; see also [70]. It proves the convergence of the Landweber scheme with a Hilbert projection.

Let X and Y be Hilbert spaces and $F : K \times (\underline{\omega}, \overline{\omega}) \to Y$ be a differentiable map where K is a convex subset of X. Let $\langle \, , \, \rangle_X$ and $\langle \, , \, \rangle_Y$ denote the scalar products in X and Y, respectively.

We are interested in solving the equation

$$F[x_*; \omega] = 0 \quad \text{for all } \omega \in (\underline{\omega}, \overline{\omega}). \tag{B.1}$$

It is natural to minimize

$$J[x] = \frac{1}{2} \int_{\underline{\omega}}^{\overline{\omega}} \| F[x; \omega] \|_Y^2 d\omega, \tag{B.2}$$

with $x \in K$. Assume that $F[\cdot; \omega]$ is Fréchet differentiable. So is J. The derivative of J is given by

$$\begin{aligned} DJ[x](h) &= \int_{\underline{\omega}}^{\overline{\omega}} \langle DF[x; \omega](h), F[x; \omega] \rangle_Y d\omega \\ &= \int_{\underline{\omega}}^{\overline{\omega}} \langle h, DF[x; \omega]^*(F[x; \omega]) \rangle_X d\omega, \end{aligned}$$

where the superscript * indicates the dual map. The iteration sequence due to the descent gradient method is given by

$$x_{n+1} = T[x_n] - \mu \int_{\underline{\omega}}^{\overline{\omega}} DF[T[x_n]; \omega]^*(F[T[x_n]; \omega]) \, d\omega. \tag{B.3}$$

Here, μ is a small number and $T[x] \in K$ is an approximation of the Hilbert projection of X onto $\overline{K}$

$$P : X \ni x \mapsto \operatorname{argmin}\{ \| x - a \| : a \in \overline{K} \}. \tag{B.4}$$

Without loss of generality, we can assume that

$$\|T[x_n] - P[x_n]\|_X \leq 2^{-n}, \quad n \geq 1.$$

The presence of T in (B.3) is necessary because x_n might not be in K and $F[x_n]$ might not be well-defined. The map T above also increases the rate of convergence of (x_n) to x_* due to

$$\|T[x_n] - x_*\|_X \leq \|x_n - x_*\|_X + 2^{-n}, \quad n \geq 1. \tag{B.5}$$

The following proposition holds.

Proposition B.0.1. *Assume that $DF[x;\omega]$ is Lipschitz continuous and that, for all $x, h \in K$,*

$$\int_{\underline{\omega}}^{\overline{\omega}} \|DF[x;\omega](h)\|_Y^2 d\omega \geq c\|h\|_X^2. \tag{B.6}$$

Then the sequence defined in (B.3) *converges to x_* provided that x_0 is a "good" initial guess for x_* and μ is sufficiently small.*

Proof. Since $DF[x;\omega]$ is Lipschitz continuous, for all x such that $\|x - x_*\|_X < \eta$ with η being a small positive number, we have

$$\begin{aligned}
\int_{\underline{\omega}}^{\overline{\omega}} \|F[x;\omega] - F[x_*;\omega] - DF[x;\omega](x - x_*)\|_Y^2 d\omega& \\
&\leq C\eta^2 \|x - x_*\|_X^2 \\
&\leq C\eta^2 \int_{\underline{\omega}}^{\overline{\omega}} \|F[x;\omega] - F[x_*;\omega]\|_Y^2 d\omega
\end{aligned} \tag{B.7}$$

for some positive constant C. Note that we have used here (B.6) and the mean-value theorem for the second inequality above.

For all $n \geq 1$, let

$$\epsilon_n[\omega] = F[T[x_n];\omega].$$

We have

$$
\begin{aligned}
&\|x_{n+1}-x_*\|_X^2-\|x_n-x_*\|_X^2-2^{-n}\\
&\quad\le \|x_{n+1}-x_*\|_X^2-\|T[x_n]-x_*\|_X^2\\
&\quad= 2\langle x_{n+1}-T[x_n],T[x_n]-x_*\rangle_X+\|x_{n+1}-T[x_n]\|_X^2\\
&\quad\le 2\mu\int_{\underline{\omega}}^{\overline{\omega}}\langle -DF[T[x_n];\omega]^*\epsilon_n[\omega],T[x_n]-x_*\rangle_X d\omega\\
&\qquad+\int_{\underline{\omega}}^{\overline{\omega}}\langle \mu\epsilon_n[\omega],\mu DF[T[x_n];\omega]DF[T[x_n];\omega]^*(\epsilon_n[\omega])\rangle_Y d\omega\\
&\quad=\int_{\underline{\omega}}^{\overline{\omega}}\langle \epsilon_n[\omega],2\mu\epsilon_n[\omega]-2\mu DF[T[x_n];\omega](T[x_n]-x_*)\rangle_Y d\omega-\mu\int_{\underline{\omega}}^{\overline{\omega}}\|\epsilon_n[\omega]\|_Y^2 d\omega\\
&\qquad+\int_{\underline{\omega}}^{\overline{\omega}}\langle \sqrt{\mu}\epsilon_n[\omega],(-I+\mu DF[T[x_n];\omega]DF[T[x_n];\omega]^*))(\sqrt{\mu}\epsilon_n[\omega])\rangle_Y d\omega\\
&\quad\le 2\mu\left(\int_{\underline{\omega}}^{\overline{\omega}}\|\epsilon_n[\omega]\|_Y^2 d\omega\right)^{\frac{1}{2}}\left(\int_{\underline{\omega}}^{\overline{\omega}}\|\epsilon_n[\omega]-DF[T[x_n];\omega](T[x_n]-x_*)\|_Y^2 d\omega\right)^{\frac{1}{2}}\\
&\qquad-\mu\int_{\underline{\omega}}^{\overline{\omega}}\|\epsilon_n[\omega]\|_Y^2 d\omega\\
&\quad+\int_{\underline{\omega}}^{\overline{\omega}}\langle \sqrt{\mu}\epsilon_n[\omega],(-I+\mu DF[T[x_n];\omega]DF[T[x_n];\omega]^*))(\sqrt{\mu}\epsilon_n[\omega])\rangle_Y d\omega\\
&\le\quad \mu(2\sqrt{C}\eta-1)\int_{\underline{\omega}}^{\overline{\omega}}\|\epsilon_n[\omega]\|_Y^2 d\omega.
\end{aligned}
$$

Here, we have used (B.7) for the last inequality. It follows that

$$\|x_{n+1}-x_*\|_X^2+\mu(1-2\sqrt{C}\eta)\int_{\underline{\omega}}^{\overline{\omega}}\|\epsilon_n\|_Y^2 d\omega-2^{-n}\le\|x_n-x_*\|_X^2,$$

and therefore,

$$\sum_{n=1}^{\infty}\int_{\underline{\omega}}^{\overline{\omega}}\|F[T[x_n];\omega]\|_Y^2 d\omega\le\frac{\|x_0-x_*\|_X^2}{\mu(1-2\sqrt{C}\eta)}+1.$$

We now obtain the convergence of (x_n) to x_* using again the mean-value theorem and condition (B.6):

$$c\|T[x_n]-x_*\|_X^2\le\int_{\underline{\omega}}^{\overline{\omega}}\|DF[\tilde{x}_n;\omega](T[x_n]-x_*)\|_Y^2 d\omega=\int_{\underline{\omega}}^{\overline{\omega}}\|F[T[x_n];\omega]-F[x_*;\omega]\|_Y^2 d\omega\to 0$$

for some $\tilde{x}_n=tT[x_n]+(1-t)x_*$, $t\in(0,1)$. □

Appendix C

Explicit calculation of G_z in the case of a sphere

We consider in this appendix that the dimension is three and that Ω is the unit sphere. We expand G, the solution to (9.3), in spherical harmonics (Y_m^l):

$$\forall z \in \Omega,\ \forall y(1,\theta,\phi) \in \partial\Omega, \qquad G_z(y) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} g_m^{l,z}\, Y_m^l(\theta,\phi).$$

An addition theorem [2, Formula (10-1-45/46)] gives us the expansion of Γ:

$$\forall z(r',\theta',\phi') \in \Omega, \forall y \in \partial\Omega, \quad \Gamma_z(y) = ik \sum_{l=0}^{\infty} \sum_{m=-l}^{l} j_l(ikr')\, h_l^{(1)}(ik) Y_m^l(\theta',\phi')\, Y_m^l(\theta,\phi),$$

where j_l and $h_l^{(1)}$ are respectively the spherical Bessel and Hankel functions of first kind of order l.

We then express the operators $\mathcal{S}_\Omega$ and $\mathcal{K}_\Omega$ in terms of spherical harmonics [102], in the same way we wrote their Fourier coefficients in the previous section:

$$\begin{aligned}
\forall y \in \partial\Omega, \qquad & (-\frac{I}{2} + \mathcal{K}_\Omega)[q](y) &&= -\sum_{l=0}^{\infty} \sum_{m=-l}^{l} k^2\, j_l'(ik)\, h_l^{(1)}(ik)\, q_m^l\, Y_m^l(\theta,\phi),\\
\forall y \in \partial\Omega, \qquad & \mathcal{S}_\Omega[q](y) &&= i \sum_{l=0}^{\infty} \sum_{m=-l}^{l} k\, j_l(ik)\, h_l^{(1)}(ik)\, q_m^l\, Y_m^l(\theta,\phi),
\end{aligned}$$

for

$$\forall y(1,\theta,\phi) \in \partial\Omega, \quad q(y) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} q_m^l\, Y_m^l(\theta,\phi).$$

From (9.5) we obtain

$$g_m^{l,z} = \frac{ik\, j_l(ikr')\, h_l^{(1)}(ik) Y_m^l(\theta',\phi')}{-k^2\, j_l'(k)\, h_l^{(1)}(ik) + \frac{1}{\ell}\, ik\, j_l(ik)\, h_l^{(1)}(ik)} = \frac{j_l(ikr')}{ik\, j_l'(ik) + \frac{1}{\ell}\, j_l(ik)} Y_m^l(\theta',\phi'),$$

or else, for all $z = (r', \theta', \phi') \in \Omega$ and $y = (1, \theta, \phi) \in \partial\Omega$,

$$G_z(y) = \sum_{l=0}^{\infty} \sum_{m=-l}^{l} \frac{j_l(ikr')}{ik\, j_l'(ik) + \frac{1}{\ell} j_l(ik)} Y_m^l(\theta', \phi') Y_m^l(\theta, \phi).$$

Note that we find a very similar formula as the one in 2D. The Bessel function of first kind is replaced by the spherical function of first kind, and our operator is decomposed in the spherical harmonics basis instead of the Fourier basis.

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