A survey on integral equations for bioelectric modeling

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Abstract

Many problems in bioelectric modeling can be approached through the formulation, and numerical resolution, of integral equations of the boundary element method. There has been a resurgence of interest in these surface integral methods due to the introduction of fast algorithms such as *fast multipole methods* (FMMs) in the context of bioelectricity problems.

This survey aims to give a self-contained, detailed and rigorous account of several of the existing equations in the literature. With a particular focus on integral equations given in terms of the surface charge density between interfaces of different conductivity. These integral equations have received less attention in the literature, but recently it was shown that they are more suitable to the application of FMM acceleration. This has led in turn to impressive improvements in the quality of simulations of M/EEG and brain stimulation.

We survey the major integral equations currently used, and showcase that the charge-based formulations are dual to the surface potential formulations, which have been so far more common in applications to bioelectricity. Some application examples are discussed, and we provide a summary of available software for electromagnetic modeling of the brain.

Introduction

Bioelectric modeling is concerned with determining the *total electric field* produced by the human body, in interaction with different instruments producing electric or magnetic fields. This problem has a wide range of applications, including electroencephalography (EEG) [32], [48], [53], magnetoencephalography (MEG) [32], [61], electrocardiology (ECG) [37], transcranial magnetic stimulation (TMS) [30], [51], transcranial electrical stimulation (TES) [30], and deep brain stimulation (DBS) [8], [30], among many others. Although the techniques of EEG/MEG and TMS/TES are quite different in their implementation, there is a common theoretical ground to all of them provided by the principle of Helmholtz reciprocity, see [25]

When the boundary element method (BEM) is involved, the solution to these problems is typically obtained in terms of an *integral equation*. These integral equations involve surface integrals over the interfaces between regions (also called compartments) of different conductivity or permittivity (studies on the conductivity of living tissues can be found for example in [12] or [36]). Two main types of integral equations can be found in the literature:

i. Integral equations for the surface potential $u(x)$, or its normal derivative $(\partial u/\partial n)(x)$ — the most common at present, and;

ii. Integral equations for the surface charge density $\rho(x)$ between interfaces of regions of different conductivity or permittivity.

From these quantities, one can obtain the full electric potential over the space $\mathbb{R}^3$. In the case of surface charge density the electric potential is found as a single-layer potential with density ρ; in the case of surface potential, or its normal derivative, the full electric potential is obtained by means of Green's formulas. For a single-compartment medium, both formulations have long been known in the potential theory literature, cf. for example Kress [33]. Both of them are applicable to conductive, dielectric, and magnetic media, cf. [31].

As to a multi-compartment conductive medium, historically the surface charge density formulation was the first one to be found: it first appeared in a discretized form in the paper by Gelernter and Swihart [14]. A subsequent continuous form, including time-dependent and dielectric effects, appeared in the paper by Barnard, Duck, and Lynn [1].

The first formulation in a multi-compartment medium expressed in terms of the surface potential can be found in the paper by Barr et. al. [2]. In this paper, the authors obtain integral equations for both homogeneous and non-homogeneous conductive media via a generalisation of Green's formula due to Smythe (see §3.06. in [56]). Thereafter, Geselowitz [16] used the same methods to find an additional integral equation in terms of the normal derivative of the potential, or equivalently in terms of the normal component of the electric field, see also Geselowitz's derivation for the magnetic field [15]. These equations involve double- and single-layer potentials respectively, in [34] a symmetric formulation (i.e. jointly considering single- and double-layer potentials) for nested domains is derived. The symmetric formulation has the advantage providing more accurate numerical results, an implementation of this method can be found in [19]. There

was an early attempt to employ the *fast multipole method* (FMM) (see [4], [6], [20], [22], [23], [44], [55]) to accelerate the symmetric formulation [35], which unfortunately did not generate convincing results. Two possible explanations are an insufficient performance of the FMM implementation or sub-optimality of the BEM formulation. This is in contrast to the application of FMM to the charge-based equations [9], [38]–[41], [46], [66] which has produced impressive results in large-scale models.

The potential-based formulations have the advantage of yielding the values of the potential at the surface directly, which is the relevant quantity in applications such as EEG. Their main drawback, however, is that these formulations assume the total electric field to be *conservative*, preventing its direct application to the non-conservative (solenoidal) fields of TMS. Nevertheless, we point out that this issue could be overcome using the methods of Nummenmaa et. al. in [47].

For many years, the charge-based equations seem to have received less attention than the surface potential equations [34], in part due to the fact that the charge-based equations require an additional integration step to retrieve the value of the potential at the boundaries. Recently, Makaroff et. al. [39]–[41] showed that the FMM, which provides accelerated means to compute the field of many charges at many observation points, is particularly well-suited for this formulation. FMM allows the computations to be carried more efficiently and make competition to the finite element method (FEM), this is mainly because FMM accelerated algorithms do not require the construction and storage of the matrix of the system. This enables us to solve much larger problems involving millions of facets in the segmentation of the conductivity interfaces.

The existing surface charge density descriptions do not impose any restrictions on the nature of the sources. The fundamental idea behind the charge-based integral equations seems to have first appeared, in the context of bioelectricity, in [14]. However, this idea has been used previously in high-frequency applications [3], [28], and also has found applications in acoustics [7]. We follow closely the exposition of Gelernter and Swihart:

1. When electric sources are activated, they produce an instantaneous *impressed electric field* $\mathbf{E}^i$ (not necessarily conservative), which is the field created by the sources in an infinite conducting medium, with boundary conditions unsatisfied.

2. Electric charge begins to flow immediately, subject to the impressed electric field, and accumulates at the interfaces between regions of different conductivity. In other words, the free flowing charges induce a surface charge density $\rho(x)$ at every interface.

3. The surface charge density gives rise to a *secondary electric field* $\mathbf{E}^s$ which is *conservative*, and is expressed explicitely in terms of $\rho(x)$ using Coulomb's law.

4. A *steady-state condition* is reached when the when the total electric field $\mathbf{E}(x)$, given as $\mathbf{E}(x) = \mathbf{E}^i(x) + \mathbf{E}^s(x)$, satifies all the boundary conditions.

The time required to achieve the steady-state condition in the human body is at least one order of magnitude smaller than 10^{-4} seconds, c.f. [14]. Thus, in practice we may model the problem using the quasi-static formulation of Maxwell's equations, by a sequence of "snapshots" of steady-state conditions. A detailed and rigorous analysis of the

quasi-static assumption in bioelectric problems can be found in the paper by Plonsey and Heppner [50]. We mention that the method of separating the electric field into an impressed/primary and secondary components has

In this paper we aim to survey the derivation of the majority of the aforementioned integral equations, providing the reader with the necessary mathematical preliminaries in a self-contained way. We have attempted to present the theory and derivations in a detailed and rigorous manner, so as to facilitate the reader to carry his or her own investigations and computer models. We pay special attention to the charge-based formulation, which has received less attention in the literature, despite the fact that it has a wider range of applicability. We present this charge-based formulation for a general *non-nested* geometry, see Figure 1. These geometries are necessary in several realistic modeling scenarios, such as those involving holes in the skull, fontanels in infants, or in cardiological applications.

We remark that for applications such to MEG or EEG one is typically interested in the *inverse problem* of locating the source of electrical activity within the brain. We will not discuss inverse problems here. We mention however that, due to the ill-posed nature of this problem, it is necessary to solve many *forward* problems (where the sources are assumed to be known) efficiently in order to obtain a solution to the inverse problem. The integral equations that we present here are used to solve the forward step in M/EEG.

First, we will present the main mathematical prerequisites. Then, we will give a full derivation of the surface charge density integral equations. Once this is done we will present the classic integral equations for surface potentials in the single and multiple compartment case. Whenever is appropriate, we establish the connections of these equations to the charge density equations. Finally, we discuss available software, where these methods are implemented, and their applications. The paper is organized into sections as follows:

I-A Mathematical Preliminaries: The Laplacian and its Green function;

I-B Mathematical Preliminaries: Jump relations of the potential theory;

II Derivation of a surface charge based integral equation via the jump relations of the potential theory;

III-A Integral equations for interior Poisson problems over a single-compartment medium in terms of the surface electric potential or its normal derivative;

III-B Integral equations for exterior Laplace problems over a single-compartment medium in terms of the surface electric potential or its normal derivative;

III-C III-C. Summary of surface-potential integral equations for single-compartment media, and their relation to the Representation Theorem in [34];

IV-A Derivation of surface-potential equations for multicompartment media.

IV-B A double-layer multicompartment integral equation;

IV-C A dual integral equation based on single-layer potentials, and its relationship to surface charge based equations;

IV-D A symmetric formulation;

V Software and Applications.

I-A. Mathematical Preliminaries: The Laplacian and its Green function

There are three main mathematical facts that we will require throughout our analyses:

i. The Laplacian operator Δ has a *Green function*, $G(x, y)$ which is a solution to the equation $\Delta G(x, y) = \delta(x - y)$, where $\delta(x)$ is the *Dirac delta*:

$$\delta(x) = \begin{cases} +\infty & \text{if } x = 0 \\ 0 & \text{if } x \neq 0 \end{cases}.$$

ii. Green's representation formula allows us to obtain the values of a harmonic function $u(x)$ away from the boundary ∂D of a bounded domain D in terms of its boundary values — the values of $u(x)$ and of its normal derivative on ∂D.

iii. The jump relations of the potential theory provide us with a way to compute limits and normal derivatives of a particular family of harmonic functions as we approach the boundary ∂D.

In this section, we will present results concerning the Laplacian and its green function. To be completely rigorous, one should work with the Dirac delta using the theory of distributions. The Dirac delta will only make an act of presence in a handful of situations, in particular in the proof of the jump relations of the potential theory — which is the deepest mathematical result we use. However, once we have these results at our disposal, the remaining arguments are rather elementary and easy-to-follow. For the sake of clarity in the exposition, we will use the deeper results as a "black-box" and refer to reference texts such as [5], or [45] for the harder technical results.

Recall that the *Laplacian operator* is defined for a function $u : \mathbb{R}^n \to \mathbb{R}$ as

$$\Delta u(x) = \sum_{i=1}^{n} \frac{\partial^2 u(x)}{\partial x_i^2}. \tag{1}$$

For a function $u(x, y)$ depending on two variables $x, y \in \mathbb{R}^n$, we denote by $\nabla_x u$ and $\nabla_y u$ the *gradient* of u with respect to the variables x and y respectively. Similarly $\nabla_x \cdot u$ and $\nabla_y \cdot u$ denote the *divergence* of u with respect to the variables x and y. With this, we denote the Laplacian operators with respect to x and y as $\Delta_x u = \nabla_x \cdot \nabla_x u$ and $\Delta_y u = \nabla_y \cdot \nabla_y u$. Whenever u depends only on one variable, or when the variable of differentiation is understood from context, we simply write ∇u and Δu. Unless stated otherwise, all integrals we consider will be on the variable y. In the context of integration, we denote a surface element by $ds(y)$ and a volume element by $dv(y)$.

We will say that D is a *bounded domain*, whenever D is a bounded set with a boundary ∂D which is piece-wise of class C^2. This boundary may have corners or edges, and it

is not necessarily connected. Let $n(x)$ be the outward unit normal vector to the surface ∂D at a point $x \in \partial D$. Each connected component of D is assumed to have positive measure (volume).

Associated to the Laplacian, there is a Green function $G(x, y)$ satisfying the equation

$$\Delta_y G(x, y) = \delta(x - y), \text{ for any given } x \in \mathbb{R}^n, \tag{2}$$

where δ is the Dirac delta distribution. This distribution is defined by the following (see Equation (1.3) in §1.1. of [5]),

$$\int_D \delta(x - y)u(y)dv(y) = u(x)\delta_D(x), \text{ where } \delta_D(x) = \begin{cases} 1 & \text{if } x \in D \\ 0 & \text{if } x \notin D \end{cases}. \tag{3}$$

The Green function of the Laplacian depends on the dimension n that we consider. We have the following result,

Theorem 1 (cf. Annexe 2.2., [5])**.** *The Green function for the Laplacian on* $\mathbb{R}^3$ *is given by*

$$G(x, y) = -\frac{1}{4\pi}\frac{1}{|x - y|}. \tag{4}$$

We will only consider equations on 3D-space, so we fix once and for all $G(x, y) := -1/(4\pi|x - y|)$. We remark that in [5] the definition of the Green function is given by $\Delta_y G(x, y) + \delta(x - y) = 0$ instead. In this case the solution is

$$\Phi(x, y) := -G(x, y) = \frac{1}{4\pi}\frac{1}{|x - y|}, \text{ for all } x \neq y \text{ in } \mathbb{R}^3. \tag{5}$$

The function $\Phi(x, y)$, also known as the *fundamental solution to the Laplace equation*, is more common in the potential theory and electromagnetism literature (e.g. in [33],[43],[56]). So, in what follows we will completely forget about $G(x, y)$ and work with $\Phi(x, y)$ instead.

From the definition of Green's function (Equation (2)), we have the following

Corollary 1. *Let* D *be an open domain of* $\mathbb{R}^3$*, and let* $u : D \to \mathbb{R}$*. If* $x \in D$*, then*

$$-u(x) = \int_D u(y)\Delta_y \Phi(x, y)dv(y) = \int_D u(y)\Delta_y \frac{1}{4\pi|x - y|}dv(y). \tag{6}$$

The Green function for the Laplacian will play a fundamental role in the study of boundary value problems. It is worth noting that, more generally, whenever we have a general linear differential operator $\mathcal{L}$ admitting a Green function much of the following theory holds verbatim, for more see §1.1. in [5].

I-B. Mathematical Preliminaries: Jump relations of the potential theory

Now we introduce several types of *potentials* given by integral operators. The use of the term potential is motivated by the fact that such functions arise naturally as scalar potentials for vector fields in several situations, such as electromagnetism. The single- and double-layer potentials play a particularly important role, since they appear in Green's representation formulas for C^2 functions on bounded and unbounded domains. Using the jump relations of the potential theory, we will be able to understand their behaviour over the entirety of $\mathbb{R}^3$, and this knowledge can then be used to extract integral equations for more general functions.

Definition 1 (cf. Chapter 3 of [45])**.** Let D be a bounded domain, and let $\varphi : \partial D \to \mathbb{R}$ be a continuous function on ∂D. The *single-layer potential* with continuous density φ is defined as

$$\left(\mathcal{S}(\varphi)\right)(x) = \int_{\partial D} \varphi(y)\Phi(x,y)ds(y), \text{ for all } x \in \mathbb{R}^3 \setminus \partial D. \tag{7}$$

The *double-layer potential* with continuous density φ is defined as

$$\left(\mathcal{D}(\varphi)\right)(x) = \int_{\partial D} \varphi(y)\frac{\partial \Phi(x,y)}{\partial n(y)}ds(y), \text{ for all } x \in \mathbb{R}^3 \setminus \partial D. \tag{8}$$

Given a continuous function $f : D \to \mathbb{R}$, we define the *Newtonian potential* with density f as

$$\left(\mathcal{V}(f)\right)(x) := \int_{D} f(y)\Phi(x,y)dv(y). \tag{9}$$

There is a dual to the double-layer potential, in the sense of the standard dot product in L^2, and it is given by

$$\left(\mathcal{D}^*(\varphi)\right)(x) = \int_{\partial D} \varphi(y)\frac{\partial \Phi(x,y)}{\partial n(x)}ds(y), \text{ for all } x \in \mathbb{R}^3 \setminus \partial D. \tag{10}$$

We also define the following operator:

$$\left(\mathcal{N}(\varphi)\right)(x) = \int_{\partial D} \varphi(y)\frac{\partial^2 \Phi(x,y)}{\partial n(x)\partial n(y)}ds(y), \text{ for all } x \in \mathbb{R}^3 \setminus \partial D. \tag{11}$$

Remark 1. Our notation for the Newtonian potential is not standard, we have chosen the symbol $\mathcal{V}$, because this is the only operator we introduce which is given by a volume integral.

By definition, the single- and double-layer potential are harmonic functions at every point $x \in \mathbb{R}^3 \setminus \partial D$. This is because we can take derivatives at x under the integral sign, whenever $x \notin \partial D$. The jump relations of the potential theory govern the behaviour of the single- and double-layer potential at the boundary ∂D.

Theorem 2 (Jump relations, cf. Theorems 6.14, 6.17, 6.18, and 6.19 in [33])**.** *Let D be a bounded domain. For a point $x \in \partial D$ and a function f defined on $\mathbb{R}^3 \setminus \partial D$, let*

$$f_{\pm}(x) = \lim_{h \to 0} f(x \pm hn(x)), \tag{12}$$

be the limiting values of f at the point x along the direction of the outward unit normal $n(x)$ to ∂D at x. Then,

(i) The single-layer potential $v(x)$ with continuous density φ is continuous throughout $\mathbb{R}^3$, and its values at a boundary point $x \in \partial D$ are given by the following convergent improper integral:

$$v(x) = \int_{\partial D} \varphi(y)\Phi(x,y)ds(y), \ x \in \partial D, \tag{13}$$

The normal derivative of the single-layer potential v has a jump at every point x of the boundary ∂D — its limiting values from the interior and exterior of D are given by the following formula:

$$\frac{\partial u_{\pm}}{\partial n}(x) = \int_{\partial D} \varphi(y)\frac{\partial \Phi(x,y)}{\partial n(x)}ds(y) \mp \frac{1}{2}\varphi(x), \quad x \in \partial D. \tag{14}$$

(ii) The double-layer potential $v(x)$ with continuous density ψ has a jump at every point of the boundary ∂D — its limiting values from the interior and exterior of D are given by the following formula:

$$v_{\pm}(x) = \int_{\partial D} \psi(y)\frac{\partial \Phi(x,y)}{\partial n(y)}ds(y) \pm \frac{1}{2}\psi(x), \quad x \in \partial D. \tag{15}$$

The normal derivative of the double-layer potential v is continuous across ∂D.

II. Derivation of a surface charge based integral equation via the jump relations of the potential theory

We derive a continuous version of the Gelernter–Swihart equations [14], which recently appeared in [39] and is equivalent to the charge-based equations in [1], after ignoring the time-dependent effects. We will only require the jump relations of the potential theory, and a few physical arguments. However, to be absolutely precise, it is necessary to describe very carefully our domains of integrations and notational conventions:

Let $D \subseteq \mathbb{R}^3$ be an *inhomogeneous* conductive volume. By this, we mean a bounded region of space which can be partitioned into several regions of *constant* electric conductivity:

$$D = D_1 \cup D_2 \cup \cdots \cup D_N. \tag{16}$$

Let $D_0 = \mathbb{R}^3 \setminus \overline{D}$ be the exterior of D. We denote by $S_j = \partial D_j$, the boundary (or surface) of the region D_j; for $j = 0, 1 \ldots, N$ — notice that $S_0 = \partial D$. The *electrical conductivity* of the region D_j is denoted by σ_j; for $j = 0, 1 \ldots, N$. The exterior region is assumed to have the conductivity of vacuum $\sigma_0 = 0$ — although in our applications the exterior medium will be air, $\sigma_0 = 0$ is a sufficient approximation. The surfaces S_j are called *surfaces of discontinuity*, or *interfaces*. We denote the union of these interfaces by

$$S = S_0 \cup S_1 \cup \cdots \cup S_N. \tag{17}$$

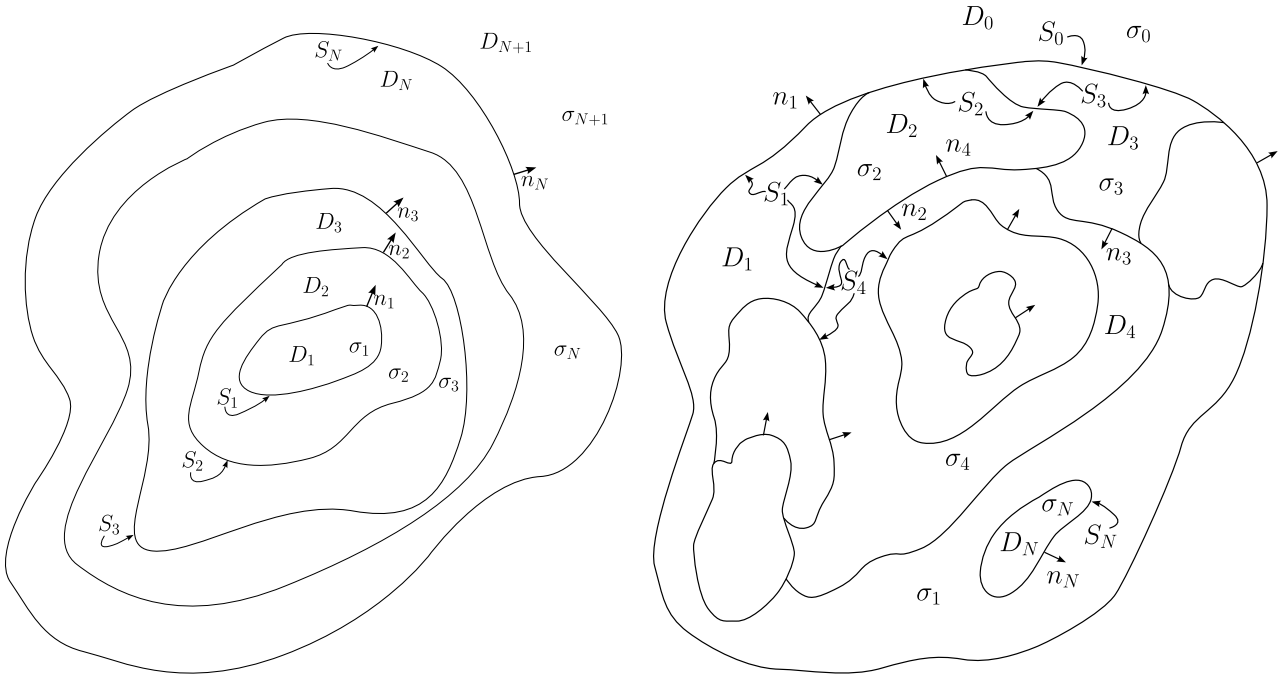
We assume that each interface S_j is piece-wise C^2 (so that there may be corners). There is a unit normal vector $n_j(x)$, pointing toward the exterior of D_j, defined almost everywhere on $x \in S_j$. It is important to note that the regions D_j may be *non-nested*, i.e. there may be two regions D_i and D_j none of them completely surrounding the other.

Remark 2. For now, we will consider general topologies and adhere to the notation set above. Later, when we consider nested compartments, it will be more convenient to enumerate the compartments from the innermost to the outermost as $D_1, D_2, \ldots, D_N$, and to let $D_{N+1} = \mathbb{R}^3 \setminus \overline{D}$ instead of D_0, (see Figure 1(a)). This ensures that n_j always points to the exterior of D_j in the nested topologies.

For notational convenience, we would like to define a normal vector $n(x)$ on every point of S. Suppose that $x \in S$ belongs only to one surface of discontinuity S_j, then we simply denote $n(x) := n_j(x)$. Whenever x belongs to the interesection of two surfaces of discontinuity, say S_i and S_j, we may choose $n(x)$ to be either the normal vector $n_i(x)$ or $n_j(x)$. In a non-nested geometry we may have $n_i(x) = -n_j(x)$, so our choice of $n(x)$ is not always unique. Our results will hold true for an arbitrary choice of normal vectors. Hence, in what follows, fix a choice of $n(x)$ once and for all.

Remark 3. Whenever x belongs to a corner of S_j, there is no well-defined normal vector n_j to the surface S_j. For now, we will restrict our analysis to those points where n_j is well defined. Later, we will explain how to complete the analysis at the corner points.

We will make use of the following notation: For a point x belonging to an interface S_j and a function f, we denote



(a) Nested topology

(b) Non-nested topology

Figure 1: Nested and non-nested topologies

$$f_{\pm}(x) = \lim_{h \to 0} f(x \pm h \cdot n(x)). \tag{18}$$

Finally, we set our notation for surface integrals: Let X be a finite union of (not necessarily closed) surfaces. Whenever we write a surface integral $\int_X f(y)ds(y)$ over X, we will count overlapping regions of different surfaces in X only once. In particular, this will hold true for surface integrals over $S = S_0 \cup \cdots \cup S_N$, and surface integrals involving the normal components of the surfaces S_j will be taken according our choice of $n(x)$.

We consider the following *forward* problem: given the knowledge of *electrical sources* within the volume D (or on its exterior D_0) at a given time t, find the *total electric field* $\mathbf{E}(x;t)$ at every point x of the space $\mathbb{R}^3$ at time t. Consider the instant t to be fixed, we will drop the dependence of all functions on the time variable. Our physical assumptions are listed below:

i. The behaviour of the total electric field is governed by the *quasi-static Maxwell equations*, see [56].

ii. The normal component of the total current through the volume D is continuous across each interface S_j, i.e. for $x \in S_j$, we have that $\mathbf{J}_+(x) \cdot n_j(x) = \mathbf{J}_-(x) \cdot n_j(x)$. In terms of the total electric field:

$$\sigma_+(x)\mathbf{E}(x) \cdot n(x) = \sigma_-(x)\mathbf{E}(x) \cdot n(x),$$

where $\sigma_{\pm}(x)$ denotes the conductivity on each side of S at the point x.

As in [14] and [39], we carry our derivation by splitting the total electric field into two components:

i. An *impressed* (or *primary*) electric field $\mathbf{E}^i$ — continuous everywhere in $\mathbb{R}^3$ and which exists independently of the domain D;

ii. A steady-state *secondary* electric field $\mathbf{E}^s$, which is a response to the primary electric field. It is generated by surface charges $\rho(x)$ on S induced by the primary electric field, and characterized by the fact that the total electric field

$$\mathbf{E}(x) = \mathbf{E}^s(x) + \mathbf{E}^i(x),$$

satisfies all boundary conditions.

The existence of surface charges at the interfaces is a straightforward physical fact: the free charges within the volume D are displaced when subject to the electric field $\mathbf{E}^i$, and accumulate at the interfaces of regions of different conductivity.

The primary electric field can be of several different types. For example, in the *forward* problem of *electroenchephalography* (EEG) the field $\mathbf{E}^i$ is given by the current dipole model of neuron activation, see [27]. Namely, $\mathbf{E}^i$ is a *conservative* field obtained from an impressed current density $\mathbf{J}^i$ via the formula $\sigma\mathbf{E}^i(x) = \mathbf{J}^i(x)$ for $x \in \mathbb{R}^3$, where (everywhere on $\mathbb{R}^3$) σ is the conductivity of gray matter. In the problem of *transcranial magnetic stimulation* (TMS) we consider a *solenoidal* vector field $\mathbf{E}^i$ given by Faraday's law of induction.

Recall that for $S = S_0 \cup S_1 \cup \cdots \cup S_N$, we define a surface integral on S as the sum of surface integrals on each S_j, counting each intersection between interfaces S_i and S_j exactly once. By Coulomb's law, we have that the secondary field is given by,

$$\mathbf{E}^s(x) = \int_S \frac{\rho(y)}{4\pi\varepsilon_0} \frac{x-y}{|x-y|^3} ds(y), \text{ for every } x \in \mathbb{R}^3, \tag{19}$$

where the constant ε_0 is the *vacuum permittivity*. Define

$$u(x) = \int_S \frac{\rho(y)}{\varepsilon_0} \Phi(x,y) ds(y), \tag{20}$$

where $\Phi(x,y) = \frac{1}{4\pi}\frac{1}{|x-y|}$ is the *fundamental solution of the Laplace equation*. We can take the gradient with respect to the variable x inside of the integral to find

$$\begin{aligned} \nabla_x u(x) = \nabla_x \int_S \frac{\rho(y)}{\varepsilon_0} \Phi(x,y) ds(y) &= \int_S \frac{\rho(y)}{\varepsilon_0} \nabla_x \Phi(x,y) ds(y) \\ &= \int_S \frac{\rho(y)}{\varepsilon_0} \nabla_x \left[\frac{1}{4\pi|x-y|} \right] ds(y) \\ &= \int_S \frac{\rho(y)}{\varepsilon_0} \left[-\frac{1}{4\pi} \frac{x-y}{|x-y|^3} \right] ds(y). \end{aligned} \tag{21}$$

Hence, $\mathbf{E}^s(x) = -\nabla u(x)$, and the field $\mathbf{E}^s$ is conservative with scalar potential $u(x)$ given by Equation (20). The normal component of $\mathbf{E}^s$ is then given by the negative of the *normal derivative* $\partial u/\partial n$ of the potential u, i.e.

$$-\frac{\partial u}{\partial n}(x) = -\nabla u(x) \cdot n(x) = \mathbf{E}^s(x) \cdot n(x). \tag{22}$$

We will derive a Fredholm integral equation of the second kind for the surface charge density ρ on S. We will do so by studying the values of the normal derivative of the potential $u(x)$ defined in Equation (20), and applying the jump relations. These relations cannot be applied to u directly, so we will require the following auxiliary potentials: We define the j-th auxiliary potential $u_j(x)$ to be the single-layer potential with density $\rho(x)/\varepsilon_0$ on the interface S_j, i.e.

$$u_j(x) = \int_{S_j} \frac{\rho(y)}{\varepsilon_0} \Phi(x,y) ds(y), \text{ for } x \in D_j. \tag{23}$$

Now, let $x \in S$ be a given surface point for which $n(x)$ is well-defined. Then x belongs to at least one interface, let S_j be one such interface for which $n(x) = n_j(x)$. By definition, a surface integral on S consists of the sum of surface integrals on each interface S_i, counting each intersection between multiple interfaces exactly once. Let $S' = \bigcup_{i=0}^{N} (S_i \setminus S_j)$ be the union of all interfaces, excluding their common portion with S_j. Then,

$$u(x) := \int_S \frac{\rho(y)}{\varepsilon_0} \Phi(x,y) ds(y) = u_j(x) + \int_{S'} \frac{\rho(y)}{\varepsilon_0} \Phi(x,y) ds(y). \tag{24}$$

The jump relations of applied to the single-layer potential u_j imply that

$$\begin{aligned} \frac{\partial (u_j)_\pm}{\partial n_j}(x) &= \int_{S_j} \frac{\rho(y)}{\varepsilon_0} \frac{\partial \Phi(x,y)}{\partial n_j(x)} ds(y) \mp \frac{\rho(x)}{2\varepsilon_0} \\ &= n_j(x) \cdot \int_{S_j} \frac{\rho(y)}{4\pi\varepsilon_0} \frac{x-y}{|x-y|^3} ds(y) \mp \frac{\rho(x)}{2\varepsilon_0}. \end{aligned} \tag{25}$$

Given that $x \notin S'$, the integral $\int_{S'} \rho(y)\Phi(x,y)/\varepsilon_0 ds(y)$ has no singularities. Therefore, we can take normal derivatives with respect to x under the integral sign. We obtain:

$$\frac{\partial}{\partial n(x)} \int_{S'} \frac{\rho(y)}{\varepsilon_0} \Phi(x,y) ds(y) = \int_{S'} \frac{\rho(y)}{\varepsilon_0} \Phi(x,y) ds(y), \tag{26}$$

approaching from either the positive or negative direction of $n(x)$. Notice that these equations are independent of the surface of discontinuity S_j chosen — they only depend on our initial choice of orientation for the normal vectors. Hence, combining Equations (24), (25), and (26), we find:

$$\begin{aligned} \frac{\partial u_\pm}{\partial n}(x) &= \int_S \frac{\rho(y)}{\varepsilon_0} \frac{\partial \Phi(x,y)}{\partial n(x)} ds(y) \mp \frac{\rho(x)}{2\varepsilon_0} \\ &= n(x) \cdot \int_S \frac{\rho(y)}{4\pi\varepsilon_0} \frac{x-y}{|x-y|^3} ds(y) \mp \frac{\rho(x)}{2\varepsilon_0}, \text{ for } x \in S. \end{aligned} \tag{27}$$

Now, use the fact that the normal component of the total current is continuous through the interfaces together with the fact that $\mathbf{E}(x) = \mathbf{E}^s(x) + \mathbf{E}^i(x)$, and $\mathbf{E}^s(x) = -\nabla u(x)$:

$$\begin{aligned} &\sigma_+(x)\mathbf{E}^i(x) \cdot n(x) - \sigma_+(x) n(x) \cdot \int_S \frac{\rho(y)}{4\pi\varepsilon_0} \frac{x-y}{|x-y|^3} ds(y) + \sigma_+(x) \frac{\rho(x)}{2\varepsilon_0} \\ &= \sigma_-(x)\mathbf{E}^i(x) \cdot n(x) - \sigma_-(x) n(x) \cdot \int_S \frac{\rho(y)}{4\pi\varepsilon_0} \frac{x-y}{|x-y|^3} ds(y) - \sigma_-(x) \frac{\rho(x)}{2\varepsilon_0}. \end{aligned} \tag{28}$$

From here, we conclude that

$$\frac{\rho(x)}{2\varepsilon_0} - K(x)\cdot n(x)\int_S \frac{\rho(y)}{4\pi\varepsilon_0}\frac{x-y}{|x-y|^3}ds(y) = K(x)\mathbf{E}^i(x)\cdot n(x), \text{ for all } x\in S, \tag{29}$$

where

$$K(x) = \frac{\sigma_-(x)-\sigma_+(x)}{\sigma_-(x)+\sigma_+(x)}, \tag{30}$$

is the *electric conductivity contrast* at the point $x \in S$. A mathematically identical equation can be derived for dielectric interface problems in bioelectromagnetic modeling, see [21].

Remark 4. Observe that if we reverse the orientation of the normal vector $n(x)$, then $\sigma_-(x)$ and $\sigma_+(x)$ are interchanged, causing a change in sign of the electric conductivity constant $K(x)$. Therefore, Equation (29) is independent of our choice of orientation for $n(x)$.

Remark 5. In the paper by Barnard, Duck, and Lynn [1], the authors describe a more general equation which takes into account time-dependent and dielectric effects. Their derivation shows that if time-dependent effects (Maxwell displacement currents) can be ignored, i.e. if the surface charge distribution is constant in time, then the dielectric effects only appear in the source term, see Equation (35) in [1]. Our source term (impressed electric field) is more general, in the sense that it is given in terms of the electric field instead of an electric potential using the dipole source model. Since we consider our impressed electric field as given, the argument in [1] justifies the omission of dielectric effects in our derivation.

Remark 6. We have ignored those points where $n(x)$ may not be well-defined. For such points, there is a generalization of the jump relations that addresses this issue, see §6.5. of [33]. This generalization introduces a correction term which is given by the angle between the normal vector at the junction of two regular pieces of a surface. We note however that, from the point of view of numerical computations, there is typically no need to consider the junction points. Assuming that $\rho(x)$ is constant on each of the pieces of a triangulation of the surface S, the numerical approximation takes only the contribution of the centroid of each piece.

III-A. Integral equations for interior Poisson problems over a single-compartment medium in terms of the surface electric potential or its normal derivative

Before giving a formulation of integral equations based on surface potentials for multicompartment media, we will consider the simpler single-compartment case. This will achieve two additional goals: to relate the surface charge density integral equations to the classical theory of boundary value problems (BVPs), and to introduce Green's formulas, which are the basis for the subsequent integral equations we will present. So for now, we exclude the presence of surfaces of discontinuity aside from ∂D. We will now discuss *Poisson problems*, see Chapter 2 of [5] and Chapter 6 of [33]. Large part of this material is of course well-known, but we include it here for the convenience of the reader.

We first consider problems with a source term in the interior of a bounded domain D. For given functions $f(x) \in C^2(D)$ and $g(x) \in C(\partial D)$, we pose the following problems:

Interior Dirichlet Problem: Find a function $u(x) \in C^2(D)$ satisfying

$$\begin{cases} \Delta u(x) = f(x) & \text{for all } x \in D \\ u(x) = g(x) & \text{for all } x \in \partial D \end{cases}. \tag{31}$$

Interior Neumann Problem: Find a function $u(x) \in C^2(D)$ satisfying

$$\begin{cases} \Delta u(x) = f(x) & \text{for all } x \in D \\ \frac{\partial u(x)}{\partial n} = g(x) & \text{for all } x \in \partial D \end{cases}. \tag{32}$$

The quantity $q(x) := \partial u(x)/\partial n = n(x) \cdot \nabla_x u(x)$ is known as the *flux* of u through the surface ∂D.

The so-called *exterior Dirichlet and Neumann problems* are analogous to the interior ones, but we consider instead an unbounded domain $\mathbb{R}^3 \setminus \overline{D}$ in place of D everywhere. Additionally, the exterior problems typically require assumptions on the asymptotic behaviour of u and f. We will consider the exterior problems separately in the following section.

Theorem 3 (Uniqueness of solutions for interior Poisson problems)**.** *There is at most one solution to the interior Dirichlet problem. Any two solutions to the interior Neumann problem differ by an additive constant.*

Proof. The claim holds true for solutions to the Laplace equation $\Delta u = 0$ by Theorems 6.11 and 6.12 in [33]. If u_1 and u_2 are two solutions to the Dirichlet problem $\Delta u = f$ on D with $u = g$ on ∂D, then $\Delta(u_1 - u_2) = 0$, and $u_1 - u_2 = 0$ on ∂D. By the maximum-minimum principle (Theorem 6.8 [33]) any function satisfying $\Delta u = 0$ on a domain D attains its minimum and maximum on the boundary ∂D, hence $u_1(x) - u_2(x) = 0$ for every $x \in D$. Similarly, if $(\partial u_i/\partial n)(x) = g(x)$ on ∂D for $i = 1, 2$, then $(\partial(u_1 - u_2)/\partial n)(x) = 0$ on ∂D, so $u_1 - u_2$ is a constant. □

There is a *reciprocity formula* associated to the Poisson problems, also known as *Green's second formula*:

Theorem 4 (Green's second formula, cf. §2.1. Identité de Réciprocité [5])**.** *Let D be a bounded domain with boundary ∂D. Let u_1 and u_2 be two C^2 functions, then*

$$\int_{\partial D} \left[u_1 \frac{\partial u_2}{\partial n} - u_2 \frac{\partial u_1}{\partial n} \right] ds = \int_D \left[u_1 \Delta u_2 - u_2 \Delta u_1 \right] dv. \tag{33}$$

Proof. Recall that Gauss' divergence theorem states that for a function ϕ,

$$\int_D \nabla \cdot \phi \; dv = \int_{\partial D} \phi \cdot n \; ds. \tag{34}$$

Now, apply Equation (34) to the function $\phi = u_2 \nabla u_1$, to obtain *Green's first formula*:

$$\int_D \nabla u_1 \nabla u_2 \; dv + \int_D u_2 \Delta u_1 \; dv = \int_{\partial D} u_2 \frac{\partial u_1}{\partial n} \; ds. \tag{35}$$

Exchange the roles of u_1 and u_2 to obtain

$$\int_D \nabla u_1 \nabla u_2 \; dv + \int_D u_1 \Delta u_2 \; dv = \int_{\partial D} u_1 \frac{\partial u_2}{\partial n} \; ds. \tag{36}$$

Finally, subtract Equation (35) from Equation (36) to obtain Equation (33). □

The reciprocity formula in Equation (33) can be used to obtain the following representation theorem for solutions to the Poisson equation:

Theorem 5 (Green's representation formula, cf. Ch. 11, §4, Eq. (5) in [43])**.** *Let D be a bounded domain and u a C^2 function in D, continuous on ∂D, then for every x in the interior of D,*

$$u(x) = \int_{\partial D} \left[\frac{\partial u}{\partial n}(y) \Phi(x,y) - u(y) \frac{\partial \Phi(x,y)}{\partial n(y)} \right] ds(y) - \int_D \Delta u(y) \Phi(x,y) dv(y), \tag{37}$$

where the rightmost integral exists as an improper integral.

Proof. Apply Equation (33) to the functions $u_1(y) := \Phi(x,y)$ and $u_2(y) := u(x)$ to obtain

$$\begin{aligned} &\int_{\partial D} \left[\frac{\partial u(y)}{\partial n} \Phi(x,y) - u(y) \frac{\partial \Phi(x,y)}{\partial n(y)} \right] ds(y) \\ &= \int_D \left[\Phi(x,y) \Delta u(y) - u(y) \Delta_y \Phi(x,y) \right] dv(y). \end{aligned} \tag{38}$$

Use the fact that $\Delta_y \Phi(x,y) = -\Delta_y G(x,y) = -\delta(x-y)$ to conclude that $u(x) = \int_D -u(y) \Delta_y \Phi(x,y) dv(y)$. From here, Equation (37) follows. □

Recall that a C^2 function u defined over an open subset D of $\mathbb{R}^3$ is called *harmonic* whenever $\Delta u(x) = 0$ for every $x \in D$.

Corollary 2 (Green's representation for harmonic functions, cf. Theorem 6.5 in [33])**.** *Let D be a bounded domain and u a harmonic function on D, continuous on ∂D, then for every x in the interior of D:*

$$u(x) = \int_{\partial D} \left[\frac{\partial u}{\partial n}(y) \Phi(x,y) - u(y) \frac{\partial \Phi(x,y)}{\partial n(y)} \right] ds(y). \tag{39}$$

Now that we have a representation formula for the values of u in the interior of D, we turn to find a formula for its values at its boundary. Assume that u is continuous along the boundary ∂D, and that its normal derivative $\partial u/\partial n$ is defined and continuous everywhere on ∂D. We can easily extend Green's representation formula for $u(x)$ to the boundary ∂D using the jump relations of the potential theory.

Since u and $\partial u/\partial n$ are continuous in the boundary, we may identify the first two integrals in Green's representation formula (Equation (37)) as single- and double-layer potentials, namely:

$$\begin{aligned} &\int_{\partial D} \frac{\partial u}{\partial n}(y)\Phi(x,y)ds(y) = \left(\mathcal{S}(\partial u/\partial n)\right)(x), \text{ and} \\ &\int_{\partial D} u(y)\frac{\partial \Phi(x,y)}{\partial n(y)}ds(y) = \left(\mathcal{D}(u)\right)(x). \end{aligned} \tag{40}$$

Thus, Equation (37) can be rewritten as:

$$u(x) = \left(\mathcal{S}(\partial u/\partial n)\right)(x) - \left(\mathcal{D}(u)\right)(x) - \left(\mathcal{V}(\Delta u)\right)(x), \text{ for every } x \in D. \tag{41}$$

Now, let $x \in \partial D$ be a point of the boundary. We consider the limit of the function u in Equation (41) as we approach x from the interior, term by term. From the jump relations (Theorem 2), we have that the single-layer potential $\mathcal{S}(\partial u/\partial n)$ is continuous at x, so

$$\lim_{h\to 0}\left(\mathcal{S}(\partial u/\partial n)\right)(x - hn(x)) = \int_{\partial D}\frac{\partial u}{\partial n}(y)\Phi(x,y)ds(y), \tag{42}$$

where the integral in the right-hand-side is a convergent improper integral. On the other hand, the double-layer potential $\mathcal{D}(u)$ has a jump at x, and the limiting value from the interior is given by Equation (15):

$$\lim_{h\to 0}\left(\mathcal{D}(u)\right)(x - hn(x)) = \int_{\partial D} u(y)\frac{\partial \Phi(x,y)}{\partial n(y)}ds(y) + \frac{1}{2}u(x). \tag{43}$$

Finally, the limit of the Newtonian potential exists as an improper integral,

$$\lim_{h\to 0}\left(\mathcal{V}(\Delta u)\right)(x - hn(x)) = \int_D \Delta u(y)\Phi(x,y)dv(y). \tag{44}$$

See Section 2.2. in [5] for more details. Combining these limit equations, we find that

$$\begin{aligned} u_-(x) = \frac{1}{2}u(x) &- \int_{\partial D} u(y)\frac{\partial \Phi(x,y)}{\partial n(y)} + \int_{\partial}\frac{\partial u}{\partial n(y)}\Phi(x,y)ds(y) \\ &- \int_D \Delta u(y)\Phi(x,y)ds(y). \end{aligned} \tag{45}$$

If we assume that u can be extended continuously from D to $\overline{D}$, then $u_-(x) = \lim_{h\to 0} u(x - hn(x)) = u(x)$, so we may rearrange the above equation to obtain:

$$\begin{aligned} &u(x) + 2\int_{\partial D} u(y)\frac{\partial \Phi(x,y)}{\partial n(y)}ds(y) \\ &\quad = 2\int_{\partial D}\frac{\partial u(y)}{\partial n}\Phi(x,y)ds(y) - 2\int_D \Delta u(y)\Phi(x,y)dv(y). \end{aligned} \tag{46}$$

We can use this equation to obtain integral equations to solve the interior Poisson problems.

Theorem 6 (Interior Neumann integral equation)**.** *Suppose that $u(x)$ is a solution to the interior Neumann Poisson problem: $\Delta u(x) = f(x)$ on D and $(\partial u/\partial n)(x) = g(x)$ on ∂D. Then, for all $x \in \partial D$, the values of u satisfy the following (Fredholm type II) integral equation:*

$$u(x) + 2\int_{\partial D} u(y)\frac{\partial \Phi(x,y)}{\partial n(y)}ds(y) = 2\int_{\partial D} g(y)\Phi(x,y)ds(y) - 2\int_D f(y)\Phi(x,y)dv(y). \quad (47)$$

Proof. Suppose that $u(x)$ is a solution to the interior Poisson problem, and apply Equation (46) to the solution $u(x)$. Substituting $\partial u/\partial n = g$ on ∂D, and $\Delta u = f$ on D, the result follows. □

Remark 7. Notice that by Gauss's divergence theorem applied to ∇u, we have that $\int_D \Delta u dv = \int_{\partial D} \nabla u \cdot n ds = \int_{\partial D}(\partial u/\partial n)ds$. Therefore, a necessary condition to the solvability of the interior Neumann problem is:

$$\int_D f(y)dv(y) = \int_{\partial D} g(y)ds(y). \quad (48)$$

By Theorem 3, any two solutions of the interior Neumann problem differ by an additive constant. Therefore, up to a constant, a solution $u(x)$ to the interior Neumann problem can be found by solving for the boundary values of u with Equation (47) (which is a Fredholm equation of the second kind) and then retrieving the interior values of u using Equation (37). This lack of uniqueness is not important in bioelectric applications, since in that case u will represent an electric potential, and the electric field $\mathbf{E} = -\nabla u$ is unaffected by the addition of a constant to u.

To obtain an integral equation for the interior Dirichlet problem we will need to compute the normal derivative of Equation (46). This normal derivative can be computed using the jump relations.

Theorem 7 (Interior Dirichlet integral equation)**.** *Suppose that $u(x)$ is a solution to the interior Dirichlet problem $\Delta u(x) = f(x)$ on D, and $u(x) = g(x)$ on ∂D. Then, the normal derivative $q(x) := (\partial u/\partial n)(x)$ of u satisfies the following (Fredholm type I) integral equation for every x on the boundary ∂D:*

$$\int_{\partial D} q(y)\frac{\partial \Phi(x,y)}{\partial n(x)}ds(y) = \int_{\partial D} g(y)\frac{\partial^2 \Phi(x,y)}{\partial n(x)\partial n(y)}ds(y) - \int_D f(y)\frac{\partial \Phi(x,y)}{\partial n(x)}dv(y). \quad (49)$$

Proof. Take normal derivatives with respect to the variable x in Equation (46) and use the fact that $\Delta u(x) = f(x)$ on D, and $u(x) = g(x)$ on ∂D. Writing $q(x) := (\partial u/\partial n)(x)$, we arrive at the following equation:

$$\begin{aligned} q(x) + 2\frac{\partial}{\partial n(x)}\int_{\partial D} g(y)\frac{\partial \Phi(x,y)}{\partial n(y)}ds(y) \\ = 2\frac{\partial}{\partial n(x)}\int_{\partial D} q(y)\Phi(x,y)ds(y) - 2\frac{\partial}{\partial n(x)}\int_D \Delta f(y)\Phi(x,y)dv(y). \end{aligned} \quad (50)$$

By the jump relations, Theorem 2, the second layer potential with continuous density $g(y)$ has a continuous normal derivative, hence we can introduce the normal derivative under the integral sign to obtain

$$\frac{\partial}{\partial n(x)} \int_{\partial D} g(y) \frac{\partial \Phi(x,y)}{\partial n(y)} ds(y) = \int_{\partial D} g(y) \frac{\partial^2 \Phi(x,y)}{\partial n(x) \partial n(y)} ds(y). \tag{51}$$

On the other hand, the single-layer potential with density $q(y)$ has a discontinuous normal derivative and the limiting value from the interior of D is given by Equation (14). So we have,

$$\frac{\partial}{\partial n(x)} \int_{\partial D} q(y) \Phi(x,y) ds(y) = \int_{\partial D} q(y) \frac{\partial \Phi(x,y)}{\partial n(x)} ds(y) + \frac{1}{2} q(x). \tag{52}$$

Combining Equations (50), (51), and (52), we find the sought Equation (49). □

We conclude this section with the observation that we can retrieve Equation (29) in the single-compartment case by the resolution of an interior Neumann boundary value problem. We will require the following,

Theorem 8 (cf. Theorem 6.25 in [33])**.** *The single-layer potential $u(x) = (\mathcal{S}(\psi))$ on D with continuous density ψ is a solution to the interior Neumann Laplace problem ($\Delta u(x) = 0$ on D, and $(\partial u/\partial n)(x) = g(x)$ on ∂D), provided that ψ is a solution to the (Fredhilm type II) integral equation:*

$$\psi(x) + 2 \int_{\partial D} \psi(y) \frac{\partial \Phi(x,y)}{n(x)} ds(y) = 2g(x), \text{ for all } x \in \partial D. \tag{53}$$

Recall that the steady-state secondary field $\mathbf{E}^s(x)$ is conservative, with potential given by $u(x) = (\mathcal{S}(\rho/\varepsilon_0))(x)$. We can extract a Neumann-type boundary condition from the assumption on continuity of the normal component of the total electric current. On a single-compartment conducting medium of electric conductivity $\sigma \neq 0$ and exterior of electric conductivity $\sigma_0 = 0$, this translates to

$$\sigma(\mathbf{E}^s(x) + \mathbf{E}^i(x)) \cdot n(x) = 0, \text{ for all } x \in \partial D. \tag{54}$$

Thus, the boundary condition for the potential $u(x)$ is $g(x) = \mathbf{E}^i(x) \cdot n(x)$, since $\mathbf{E} \cdot n = -\partial u/\partial n$. Now, applying Theorem 8 to $u(x)$ we find the integral equation

$$\frac{\rho(x)}{2\varepsilon_0} - n(x) \cdot \int_{\partial D} \frac{\rho(y)}{4\pi\varepsilon_0} \frac{x-y}{|x-y|^3} ds(y) = \mathbf{E}^i(x) \cdot n(x), \text{ for all } x \in \partial D. \tag{55}$$

Note that since the electric conductivity contrast is $K(x) = \frac{\sigma - 0}{\sigma + 0} = 1$ everywhere, the equation above agrees with Equation (29).

III-B. Integral equations for exterior Laplace problems over a single-compartment medium in terms of the surface electric potential or its normal derivative

The *exterior Poisson problems* are considered over $\mathbb{R}^3 \setminus \overline{D}$, where D is a bounded domain. For simplicity, we only consider the *Laplace equation*, i.e. the Poisson equation with no sources, so that $f = 0$. The added complication for exterior problems resides in the fact that we must impose restrictions on the asymptotic behaviour of our sources and solutions. The Laplace equation suffices for many applications, and we will later develop a general multicompartment formulation, so we refer the reader to §2.3 in [5] for a general treatment.

Exterior Dirichlet Problem Given a bounded domain D and a continuous function $g : \partial D \to \mathbb{R}$, find a C^2 function u such that

$$\begin{cases} \Delta u = 0 & \text{on } \mathbb{R}^3 \setminus \overline{D} \\ u = g & \text{on } \partial D \end{cases}, \tag{56}$$

furthermore, we require that $u(x) = o(1)$ as $|x| \to \infty$.

Exterior Neumann Problem Given a bounded domain D and a continuous function $g : \partial D \to \mathbb{R}$, find a C^2 function u such that

$$\begin{cases} \Delta u = 0 & \text{on } \mathbb{R}^3 \setminus \overline{D} \\ \frac{\partial u}{\partial n} = g & \text{on } \partial D \end{cases}, \tag{57}$$

furthermore, we require that $u(x) = o(1)$ as $|x| \to \infty$.

Theorem 9 (cf. Theorems 6.11 and 6.12 in [33])**.** *The exterior Dirichlet and Neumann Laplace problems have a unique solution.*

Theorem 10 (Exterior Green representation theorem, cf. Theorem 6.10 [33])**.** *Let D be a bounded domain, and let $n(x)$ be the outward unit normal to $x \in \partial D$ directed toward the exterior of D. Suppose that u is a C^2 function in $D^c := \mathbb{R}^3 \setminus \overline{D}$, with $\Delta u(x) = 0$ everywhere in $\mathbb{R}^3 \setminus \overline{D}$, and that $u(x) = o(1)$ as $|x| \to \infty$. Then, for every x in the interior of D^c*

$$u(x) = \int_{\partial D} \left[u(y) \frac{\partial \Phi(x,y)}{\partial n(y)} - \frac{\partial u}{\partial n}(y) \Phi(x,y) \right] ds(y). \tag{58}$$

Remark 8. Notice that Equation (58) is identical to Equation (39). The change of sign is accounted by the fact that an outward normal to D is an inward normal to $\mathbb{R}^3 \setminus \overline{D}$.

Using the jump relations we can also obtain integral equations to solve the exterior problems. Let $u(x)$ be harmonic on $\mathbb{R}^3 \setminus \overline{D}$, and suppose that $u(x)$ is continuous on ∂D and has a continuous normal derivative $(\partial u/\partial n)(x)$ on ∂D. Then, we can identify the integrals in Equation (58) as single- and double-layer potentials, and write

$$u(x) = \mathcal{D}(u)(x) - \mathcal{S}(\partial u/\partial n)(x), \text{ for all } x \in \mathbb{R}^3 \setminus \overline{D}. \tag{59}$$

Now, let $x \in \partial D$ be given — we will compute the limit of u in the above expression at x approaching from the exterior. From the jump relations (Theorem 2), we have that the double-layer potential with continuous density $u(x)$ can be extended continuously from $\mathbb{R}^3 \setminus \overline{D}$ to ∂D, with limiting values given by Equation (15). This implies that approaching from the exterior,

$$\lim_{h \to 0} \mathcal{D}(u)(x + hn(x)) = \int_{\partial D} u(y) \frac{\partial \Phi(x,y)}{\partial n(y)} ds(y) + \frac{1}{2} u(x) \tag{60}$$

On the other hand, the jump relations imply that the single-layer potential with continuous density $\varphi(x) = (\partial u/\partial n)(x)$ is continuous throughout $\mathbb{R}^3$. Hence,

$$\lim_{h \to 0} \mathcal{S}(\partial u/\partial n)(x + hn(x)) = \int_{\partial D} \frac{\partial u}{\partial n}(y) \Phi(x,y) ds(y). \tag{61}$$

Combining these limit equations, we find

$$u_+(x) = \frac{1}{2} u(x) + \int_{\partial D} u(y) \frac{\partial \Phi(x,y)}{\partial n(y)} ds(y) - \int_{\partial D} \frac{\partial u}{\partial n}(y) \Phi(x,y) ds(y). \tag{62}$$

If u can be extended continuously from $\mathbb{R}^3 \setminus \overline{D}$ to $\mathbb{R}^3 \setminus D$, then $u_+(x) = \lim_{h \to 0} u(x + hn(x)) = u(x)$, in which case we find

$$u(x) + 2 \int_{\partial D} \left[\frac{\partial u}{\partial n}(y) \Phi(x,y) - u(y) \frac{\partial \Phi(x,y)}{\partial n(y)} \right] ds(y) = 0. \tag{63}$$

Theorem 11 (Exterior Dirichlet integral equation)**.** *Let $u(x)$ be a solution to the exterior Dirichlet problem with boundary condition $u = g$ on ∂D. Then, its normal derivative $q(x) := (\partial u/\partial n)(x)$ at the boundary ∂D satisfies the (Fredholm type I) integral equation:*

$$\int_{\partial D} q(y) \frac{\partial \Phi(x,y)}{n(x)} ds(y) = \int_{\partial D} g(y) \frac{\partial^2 \Phi(x,y)}{\partial n(x) \partial n(y)} ds(y), \text{ for all } x \in \partial D. \tag{64}$$

Proof. Take the normal derivatives (with respect to x) in Equation (63), and substitute $u(x) = g(x)$ on ∂D to find

$$\frac{\partial u}{\partial n}(x) + 2 \frac{\partial}{\partial n(x)} \int_{\partial D} \frac{\partial u}{\partial n}(y) \Phi(x,y) ds(y) - 2 \frac{\partial}{\partial n(x)} \int_{\partial D} g(y) \frac{\partial \Phi(x,y)}{\partial n(y)} ds(y) = 0. \tag{65}$$

By the jump relations (Theorem 2), the normal derivative of the single-layer potential with continuous density $q(x) := (\partial u/\partial n)(x)$ can be extended continuously to the boundary from either the inside or outside of D, with limiting values given by Equation (14). This implies that the normal derivative from the exterior is:

$$\frac{\partial}{\partial n(x)} \int_{\partial D} \frac{\partial u}{\partial n}(y) \Phi(x,y) ds(y) = \int_{\partial D} \frac{\partial u}{\partial n}(y) \frac{\partial \Phi(x,y)}{\partial n(x)} ds(y) - \frac{1}{2} \frac{\partial u}{\partial n}(x). \tag{66}$$

Combining Equation (65) and (66), we find

$$\begin{aligned} \int_{\partial D} \frac{\partial u}{\partial n}(y) \frac{\partial \Phi(x,y)}{\partial n(x)} ds(y) &= \frac{\partial}{\partial n(x)} \int_{\partial D} g(y) \frac{\partial \Phi(x,y)}{\partial n(y)} ds(y) \\ &= \int_{\partial D} g(y) \frac{\partial^2 \Phi(x,y)}{\partial n(x) \partial n(y)}. \end{aligned} \tag{67}$$

The last equality follows from the continuity of the normal derivative of the double-layer potential. Substituting $q(x) = (\partial u/\partial n)(x)$ yields Equation (64). □

Theorem 12 (Exterior Neumann integral equation)**.** *Let $u(x)$ be a solution to the exterior Neumann problem with boundary condition $(\partial u/\partial n)(x) = g(x)$ on ∂D. Then, its value $u(x)$ at the boundary ∂D satisfies the (Fredholm type II) integral equation:*

$$u(x) - 2\int_{\partial D} u(y)\frac{\partial \Phi(x,y)}{\partial n(y)} ds(y) = -2\int_{\partial D} g(y)\Phi(x,y)ds(y), \text{ for all } x \in \partial D. \tag{68}$$

Proof. This follows directly from Equation (63) by noticing that $(\partial u/\partial n)(x) = g(x)$ on the boundary ∂D. □

III-C. Summary of surface-potential integral equations for single-compartment media, and their relation to the Representation Theorem in [34]

We give a summary of the integral equations obtained in Section III-A and Section III-B. We will express these using the operator notation $\mathcal{S}, \mathcal{D}, \mathcal{D}^*, \mathcal{N}$, and $\mathcal{V}$. Recall that, following Bonnet [5], we denote the normal derivative of $u(x)$ by $q(x) = (\partial u/\partial n)(x)$. The equations in the table below assume that u is C^2 on D or $\mathbb{R}^3 \setminus \overline{D}$ for interior or exterior problems respectively. Furthermore, we assume that u can be extended continuously to ∂D, and that $q(x) = (\partial u/\partial n)$ exists and is continuous on ∂D.

Type	PDE	Boundary condition	Integral Equation	Type	Equation number
Interior	$\Delta u = f$	$u = g$	$\mathcal{D}^*(q) = \mathcal{N}(g) - \mathcal{V}(f)$	I	Eq. (49)
Interior	$\Delta u = f$	$q = g$	$u + 2\mathcal{D}(u) = 2\mathcal{S}(g) - 2\mathcal{V}(f)$	II	Eq. (47)
Exterior	$\Delta u = 0$	$u = g$	$\mathcal{D}^*(q) = \mathcal{N}(g)$	I	Eq. (64)
Exterior	$\Delta u = 0$	$q = g$	$u - 2\mathcal{D}(u) = -2\mathcal{S}(g)$	II	Eq. (68)

Table 1: Integral equations in terms of the potential or its normal derivative

The following theorem, which we reproduce from [34], is a variation of the equations above. It expresses a harmonic function u, or its normal derivative, in terms of their jumps at the boundary ∂D.

Theorem 13 (Representation Theorem, cf. Theorem 1 [34])**.** *Let $D \subseteq \mathbb{R}^3$ be a bounded domain with regular boundary ∂D. Let $u : \mathbb{R}^3 \setminus \partial D \to \mathbb{R}$ be a harmonic function. Then, letting $q := \partial u/\partial n$ we have*

$$\begin{aligned} -q &= +\mathcal{N}([u]) - \mathcal{D}^*([q]), \\ u &= -\mathcal{D}([u]) + \mathcal{S}([q]), \ \textit{away from } \partial D. \\ -q_\pm &= +\mathcal{N}([u]) + \left(\pm\frac{\mathcal{I}}{2} - \mathcal{D}^*\right)([q]), \\ u_\pm &= \left(\mp\frac{\mathcal{I}}{2} - \mathcal{D}\right)([u]) + \mathcal{S}([q]), \ \textit{on } \partial D, \end{aligned} \tag{69}$$

where $\mathcal{I}$ denotes the identity operator, and $[f]$ denotes the jump of f at the boundary ∂D.

To prove Theorem 13, one can use an extension of Green's identities to the boundary and Gauss's integral, see Equation (2.20) in [5] and Chapter 18, §4 of [43] for the details. Using the limiting values from the interior, we find

$$\int_{\partial D} \left[\frac{\partial u_-}{\partial n}(y)\Phi(x,y) - u_-(y)\frac{\partial \Phi(x,y)}{\partial n(y)}\right] ds(y) = \begin{cases} u(x) & \text{if } x \in D \\ \frac{1}{2}u_-(x) & \text{if } x \in \partial D \\ 0 & \text{if } x \in \mathbb{R}^3 \setminus \overline{D} \end{cases}. \tag{70}$$

Likewise, using the exterior limiting values

$$-\int_{\partial D}\left[\frac{\partial u_+}{\partial n}(y)\Phi(x,y)-u_+(y)\frac{\partial\Phi(x,y)}{\partial n(y)}\right]ds(y)=\begin{cases}u(x) & \text{if } x\in\mathbb{R}^3\setminus\overline{D}\\ \frac{1}{2}u_+(x) & \text{if } x\in\partial D\\ 0 & \text{if } x\in D\end{cases}. \tag{71}$$

We combine the last two equations to obtain

$$u(x)=\int_{\partial D}\left[\left(\frac{\partial u_-}{\partial n}(y)-\frac{\partial u_+}{\partial n}(y)\right)\Phi(x,y)-(u_-(y)-u_+(y))\,\frac{\partial\Phi(x,y)}{\partial n(y)}\right]ds(y), \tag{72}$$

for every $x\in\mathbb{R}^3\setminus\partial D$. This equation is expressed in operator notation as,

$$u=-\mathcal{D}([u])+\mathcal{S}([q]),\ \text{away from } \partial D. \tag{73}$$

Taking normal derivatives in the expression above, we find

$$q=-\mathcal{N}([u])+\mathcal{D}^*([q]),\ \text{away from } \partial D. \tag{74}$$

For a point $x\in\partial D$, we may compute the limiting values $u_\pm$ of u at x by using the jump relations of the potential theory. On the one hand, we have that

$$\lim_{h\to 0}\mathcal{S}([q])(x\pm hn(x))=\mathcal{S}([q])(x), \tag{75}$$

by the continuity of single-layer potentials. And on the other hand, Equation (15) implies,

$$\lim_{h\to 0}\mathcal{D}([u])(x\pm hn(x))=\pm\frac{1}{2}[u](x)+\mathcal{D}([u])(x). \tag{76}$$

This in turn implies

$$u_\pm=\left(\mp\frac{\mathcal{I}}{2}-\mathcal{D}\right)([u])+\mathcal{S}([q]). \tag{77}$$

The identity

$$-q_\pm=\mathcal{N}([u])+\left(\pm\frac{\mathcal{I}}{2}-\mathcal{D}^*\right)([q]), \tag{78}$$

can be shown analogously from Equation 74.

IV-A. Derivation of surface-potential equations for multicompartment media

We now turn to integral equations for the surface potential or its normal derivative in a multicompartment medium. Similar to the single-compartment case, we have formulations using single- and double-layer potentials respectively. The double-layer potential formulation follows naturally from the direct application of Smythe's generalisation of Green's representation formula due to Smythe [56], and it was first derived by Barr et. al. in [2]. The single-layer formulation, due to Geselowitz [16], follows also directly from Smythe's formula, but we apply it instead to the electric potential modified by the resistivity of the compartments. Both these formulations were obtained during the 1960s. In 2005, Kybic et. al. [34], motivated by the use of a common theoretical framework for the past integral equations, found a *symmetric* formulation that combines both single- and double-layer potentials. This symmetric formulation produces more accurate numerical results.

Smythe's formula as it was proven in [56] is only valid for nested domains, so all these formulations only apply to nested multicompartment media. It was claimed in [34] that said equations hold also true for non-nested geometries, but details were omitted. The non-nested generalization was subsequently developed in detail by Stenroos in [57]. In what follows, we will present the single- and double-layer formulations mentioned above, and sketch the proof of the symmetric formulation in [34]. We also show that from the single-layer equation of Geselowitz one can retrieve a particular case of the charge-based formulation in Equation (29).

Consider a volume D containing biolectric sources in its interior, and which is partitioned into disjoint *nested* regions (or compartments) $D_1, D_2, \ldots, D_N$ of uniform conductivity (see Figure 1(a)). Let $D_{N+1} = \mathbb{R}^3 \setminus \overline{D}$, and let $S_i = \partial D_i \setminus \partial D_{i-1}$ be the interface between the compartment D_{i-1} and the compartment D_i. Finally, let $n_j(x)$ be the unit normal vector to the surface S_j directed towards D_i at the point $x \in S_j$. Denote $n(x) := n_j(x)$, whenever $x \in S_1 \cup S_2 \cup \cdots \cup S_N \cup S_{N+1}$ belongs to the interface S_j. Recall that $f_\pm(x) = \lim_{h\to 0} f(x \pm hn(x))$ for x in a surface S, where n is the outward unit normal to S. Following Geselowitz [16] and Sarvas [52], we make the following physical assumptions:

(i) *There is a uniform bulk conductivity* σ, which is constant on each compartment D_j. Bioelectric sources are given by a *distribution of impressed current density* $\mathbf{J}^i$ — the total current is then given by the formula:

$$\mathbf{J}(x) = \sigma(x)\mathbf{E}(x) + \mathbf{J}^i(x), \text{ for all } x \in \mathbb{R}^3 \tag{79}$$

The exterior compartment is assumed to have zero conductivity, i.e. $\sigma(x) = 0$ for all $x \in D_{N+1}$.

(ii) *Electromagnetic waves can be neglected*, so

$$\mathbf{E}(x) = -\nabla u(x), \text{ for all } x \in \mathbb{R}^3, \tag{80}$$

for some scalar potential $u : \mathbb{R}^3 \to \mathbb{R}$.

(iii) We may assume that there is *no tissue capacitance*, hence

$$\nabla \cdot \mathbf{J}(x) = 0, \text{ for all } x \in \mathbb{R}^3 . \tag{81}$$

(iv) *The normal component of the total current is continuous across each boundary*: $\mathbf{J}_-(x) \cdot n_j(x) = \mathbf{J}_+(x) \cdot n_j(x)$ for all $x \in S_j$. Using (i) and (ii) we can rewrite this as,

$$\sigma_-(x)\frac{\partial u_-}{\partial n_j}(x) = \sigma_+(x)\frac{\partial u_+}{\partial n_j}(x), \text{ for all } x \in S_j. \tag{82}$$

(v) The potential is continuous on each boundary S_j:

$$u_-(x) = u_+(x), \text{ for all } x \in S_j. \tag{83}$$

The assumptions (i), (ii), and (iii) combined give

$$0 = \nabla \cdot \mathbf{J}(x) = -\sigma(x)\Delta u(x) + \nabla \cdot \mathbf{J}^i(x), \text{ for all } x \in \mathbb{R}^3 . \tag{84}$$

Denoting $[f]_j(x) = f_-(x) - f_+(x)$ for $x \in S_j$, for the jump of the function f at the surface S_j, we see that all the assumptions above are equivalent to the following problem, cf. Kybic et. al. [34]

Connected Poisson Problems. Find a C^2 function u defined on $\mathbb{R}^3$ and satisfying $u(x) = o(1)$ as $|x| \to \infty$, such that

$$\begin{cases} \sigma\Delta u = \nabla \cdot \mathbf{J}^i & \text{in } D_j, \text{ for all } j = 1, \dots, N \\ \Delta u = 0 & \text{in } D_{N+1} = \mathbb{R}^3 \setminus \overline{D} \\ [u]_j = [\sigma\frac{\partial u}{\partial n_j}]_j = 0 & \text{on } S_j, \text{ for all } j = 0, \dots, N-1 \end{cases} . \tag{85}$$

We now present Smythe's generalization of Green's formula to nested multicompartment media, which will be the main theoretical tool in this section.

Theorem 14 (Green's Multicompartment Formula, see Chapter III §3.06 in [56])**.** *Let D be a multicompartment bounded volume as above, and let $S_1, \dots, S_N, S_{N+1} = \partial D$ be the interfaces between the nested regions of D. Let $\psi, \varphi : D \to \mathbb{R}$ be C^2 functions, which are continuous on $S_{N+1} = \partial D$, and let $\sigma : D \to \mathbb{R}$ be a function which is C^1 on D except for possible discontinuities on the surfaces S_j. Then,*

$$\begin{aligned} \sum_{j=1}^{N+1} \int_{S_j} \left[\sigma_- \left(\psi_- \frac{\partial \varphi_-}{\partial n_j} - \varphi_- \frac{\partial \psi_-}{\partial n_j} \right) - \sigma_+ \left(\psi_+ \frac{\partial \varphi_+}{\partial n_j} - \varphi_+ \frac{\partial \psi_+}{\partial n_j} \right) \right] dS_j \\ = \int_D [\psi \nabla \cdot (\sigma \nabla \varphi) - \varphi \nabla \cdot (\sigma \nabla \psi)] dv. \end{aligned} \tag{86}$$

IV-B. A double-layer multicompartment integral equation

The multi-compartment integral equation in [2] gives an integral equation for the multicompartment problem which is of the Dirichlet type, i.e. where we have knowledge of the boundary values of the potential u at the discontinuity surfaces.

Fix a point x of D away from the interfaces, and substitute $\psi(y) = \Phi(x,y) = 1/(4\pi|x-y|)$, and $\varphi(y) = u(y)$ (the electric potential) in Green's multicompartment formula, (Equation (86)). Using the fact that the potential u, and the fundamental solution Φ are continuous along the interfaces (so that $u_+(y) = u_-(y) = u(y)$ and $\Phi_+(x,y) = \Phi_-(x,y) = \Phi(x,y)$ for $y \neq x$), we find the following equation:

$$\begin{aligned}
&\sum_{j=1}^{N+1} \int_{S_j} \left[\sigma_-(y) \frac{\partial u_-}{\partial n_j}(y) - \sigma_+(y) \frac{\partial u_+}{\partial n_j}(y) \right] \Phi(x,y) ds(y) \\
&- \sum_{j=1}^{N+1} \int_{S_j} (\sigma_-(y) - \sigma_+(y)) u(y) \frac{\partial \Phi(x,y)}{\partial n_j(y)} ds(y) \\
&= \int_D \left[\Phi(x,y) \nabla_y \cdot (\sigma(y) \nabla_y u(y)) - u(y) \nabla_y \cdot (\sigma(y) \nabla_y \Phi(x,y)) \right] dv(y).
\end{aligned} \tag{87}$$

We can further simplify this equation: Using the continuity of current (Equation (82)), the term $(\sigma_-(y)\partial u_-/\partial n_j(y) - \sigma_+(y)\partial u_+/\partial n_j(y))$ vanishes. The term on the right-hand-side of the equal sign is simplified as follows: Consider a sufficiently small neighbourhood B of x so that $\sigma(x)$ is constant on B. Then, by Corollary 1 we have

$$-\int_D u(y) \nabla_y \cdot (\sigma(y) \nabla_y \Phi(x,y)) dv(y) = -\int_B \sigma(x) u(y) \Delta_y \frac{1}{4\pi|x-y|} = \sigma(x) u(x). \tag{88}$$

On the other hand, from Equation (79), Equation (80), and Equation (81) we have that $\nabla \cdot \sigma \nabla u = \nabla \mathbf{J}^i$. Combining all of the above remarks, we find the following integral equation:

$$\sigma(x) u(x) = -\sum_{j=1}^{N+1} \int_{S_j} u(y) (\sigma_-(y) - \sigma_+(y)) \frac{\partial \Phi(x,y)}{\partial n_j(y)} ds(y) - \int_D \frac{\nabla_y \cdot \mathbf{J}^i(y)}{4\pi|x-y|} dv(y), \tag{89}$$

which can also be written in operator notation as:

$$\sigma u + \sum_{j=1}^{N+1} \mathcal{D}([\sigma]_j u) = -\mathcal{V}(\nabla \cdot \mathbf{J}^{\mathbf{i}}). \tag{90}$$

Notice that the great advantage of the equation above is that it provides the electric potential at each surface directly, assuming that we have knowledge of all the conductivity values and sources in the volume.

IV-C. A dual integral equation based on single-layer potentials, and its relationship to surface charge based integral equations

This time, we let $\psi(y) = \Phi(x,y) = 1/(4\pi|x-y|)$ and $\sigma(x)\phi(x) = u(x)$, in Green's multicompartment formula (Equation (86)). This yields,

$$\begin{aligned}\sum_{j=1}^{N+1}\int_{S_j}\left[\left(\frac{\partial u_-}{\partial n_j}(y) - \frac{\partial u_+}{\partial n_j}(y)\right)\Phi(x,y) - (u_- - u_+)\frac{\partial \Phi(x,y)}{\partial n_j(y)}\right]ds(y)\\ = \int_D\left[\Phi(x,y)\nabla\cdot\nabla u(y) - \frac{u(y)}{\sigma(y)}\nabla_y\cdot\sigma(y)\nabla_y\Phi(x,y)\right]dv(y).\end{aligned} \tag{91}$$

We simplify the equation above: By the continuity of the potential u, we have $u_-(y) - u_+(y) = 0$. On the other hand, Equations (79), (80), and (81) imply that $\nabla\cdot\nabla u = (1/\sigma)\nabla\cdot\mathbf{J}^i$, which gives,

$$\begin{aligned}\sum_{j=1}^{N+1}\int_{S_j}\left[\left(\frac{\partial u_-}{\partial n_j}(y) - \frac{\partial u_+}{\partial n_j}(y)\right)\Phi(x,y)\right]ds(y)\\ = \int_D\left[\Phi(x,y)\frac{\nabla\mathbf{J}^i(y)}{\sigma(y)} - \frac{u(y)}{\sigma(y)}\nabla_y\cdot\sigma(y)\nabla_y\Phi(x,y)\right]dv(y).\end{aligned} \tag{92}$$

Using Equation Corollary 1 again, we find

$$\int_D \frac{u(y)}{\sigma(y)}\nabla\cdot\sigma\nabla_y\Phi(x,y)dv(y) = -u(x). \tag{93}$$

Therefore, we obtain the equation:

$$\sum_{j=1}^{N+1}\int_{S_j}\left(\frac{\partial u_-}{\partial n_j}(y) - \frac{\partial u_+}{\partial n_j}(y)\right)\Phi(x,y)ds(y) = u(x) + \int_D \Phi(x,y)\frac{\nabla\cdot\mathbf{J}^i(y)}{\sigma(y)}dv(y). \tag{94}$$

Recall that for a function f, we denote the jump of f across the boundary S_j as $[f]_j = f_- - f_+$. In operator notation, the above equation can be rewritten as:

$$u(x) - \sum_{j=1}^{N+1}\mathcal{S}([\partial u/\partial n]_j) = \mathcal{V}(-(\nabla\cdot\mathbf{J}^i)/\sigma). \tag{95}$$

In [16], once he obtains the equation above Geselowitz proceeds to rewrite it with a term involving the electric conductivity contrast. However, we note that Geselowitz's equation involving single-layer potentials does not constitute a true dual to Equation (89), since it involves two unknowns: u and its jump $[\partial u/\partial n]_j$ at each interface. To obtain a dual, we proceed in a similar fashion as in the derivation of our Equation (29), and Equation (15) in the paper [34]. First, note that the jump relations for the single-layer potential (Equation (14)) take the following form in operator notation:

$$\frac{\partial\mathcal{S}[\varphi]_\pm}{\partial n}(x) = \mathcal{D}^*[\varphi](x) \mp \frac{1}{2}\varphi(x). \tag{96}$$

Apply the jump relations to find the normal derivative of Equation (95) from either side of S_j, and multiply the equation by σ_- and σ_+ respectively to find,

$$\begin{aligned}\sigma_\pm(x)\frac{\partial u_\pm}{\partial n_i}(x) \pm \frac{\sigma_\pm}{2}[\partial u/\partial n]_i(x) - \sum_{j=1}^{N+1}\sigma_\pm(x)\mathcal{D}^*([\partial u/\partial n]_j)(x) \\ = \sigma_\pm\frac{\partial}{\partial n_i}\mathcal{V}[-(\nabla\cdot\mathbf{J}^i)/\sigma](x),\end{aligned} \tag{97}$$

whenever $x \in S_i$. Subtracting the version of the equation above with a positive sign from the one with a negative sign, and using the continuity of the normal component of the current (Equation (82)), we obtain:

$$\frac{\sigma_- + \sigma_+}{2}[\partial u/\partial n]_i - (\sigma_- - \sigma_+)\sum_{j=1}^{N+1}\mathcal{D}^*([\partial u/\partial n]_j) = (\sigma_- - \sigma_+)\frac{\partial}{\partial n_i}\mathcal{V}[-(\nabla\cdot\mathbf{J}^i)/\sigma]. \tag{98}$$

Dividing by the value $(\sigma_- + \sigma_+)$, we can express this in terms of the electric conductivity contrast K (cf. Equation (30)) as follows:

$$\frac{1}{2}[\partial u/\partial n]_i - K\sum_{j=1}^{N+1}\mathcal{D}^*([\partial u/\partial n]_j) = K\frac{\partial}{\partial n_i}\mathcal{V}[-(\nabla\cdot\mathbf{J}^i)/\sigma] \tag{99}$$

Denoting $\xi(x) := [\partial u/\partial n]_i(x)$ for $x \in S_i$, we obtain

$$\frac{1}{2}\xi(x) - K(x)\sum_{j=1}^{N+1} n_i(x)\cdot\int_{S_j}\frac{\xi(y)}{4\pi}\frac{x-y}{|x-y|^3}ds(y) = K(x)\frac{\partial}{\partial n_i}\int_D\frac{-\nabla\cdot\mathbf{J}^i(y)}{\sigma(y)}dv(y), \tag{100}$$

Which is dual to Equation (89). The resemblance between Equation (100) and Equation (29) is not just a coincidence, in fact Equation (100) is only a particular case of Equation (29). This becomes apparent after considering units of measurement: the jump $\xi(x) = [\partial u/\partial n]_i(x)$ of the normal derivative of the potential is measured in volts per meter ($\mathbf{V}\cdot\mathbf{m}^{-1}$), whereas the surface charge density is measured in Coulombs per meter-square ($\mathbf{C}\cdot\mathbf{m}^{-2}$). The vacuum permittivity ε_0 is measured in farads per meter ($\mathbf{F}\cdot\mathbf{m}^{-1} = \mathbf{C}\cdot\mathbf{V}^{-1}\cdot\mathbf{m}^{-1}$), therefore $\rho(x)/\varepsilon_0$ and $\xi(x)$ have the same units of measurement. In fact using Gauss's law it can be shown that both quantities coincide, see §2.3.5. in Griffiths's Electrodynamics [24].

IV-D. A symmetric formulation

We conclude this section with a sketch of the derivation of the symmetric integral equations of Kybic et. al. [34], which involve a combination of single- and double-layer potentials in two unknown variables.

Again, consider a sequence of nested compartments $D_1, D_2, \ldots, D_N$, with $D = \bigcup_{i=1}^{N} D_i$ and $D_{N+1} = \mathbb{R}^3 \setminus \overline{D}$ (see Figure 1(a)). Recall that $S_i = \partial D_i \setminus \partial D_{i-1}$ is the interface between the compartment D_{i-1} and the compartment D_i, with n_i the unit normal vector at S_i directed towards D_i.

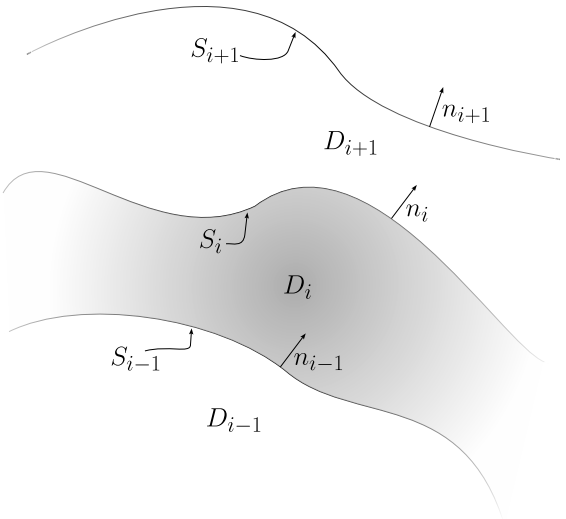


Figure 2: The compartment D_i and its adjacent compartments

To carry this derivation, the authors in [34] use three sets of potentials

- A potential u solving the connected Poisson problems of Equation (85);
- A sequence of Newtonian potentials v_i, which solve the Poisson problem restricted to the domain D_i, and which take value 0 everywhere else; and
- A sequence of harmonic functions w_i, whose jumps at the interfaces are given by the values of the potential u and its normal derivative.

The Newtonian potentials v_i are defined as:

$$v_i(x) := \mathcal{V}[-f \cdot \mathbf{1}_{D_i}](x) = \int_D [-f \cdot \mathbf{1}_{D_i}](y)\Phi(x,y)dv(y), \tag{101}$$

where $\mathbf{1}_{D_i}(x) = 1$ if $x \in D_i$ and $\mathbf{1}_{D_i}(x) = 0$ otherwise. Since $\Delta_x\Phi(x,y) = \Delta_y\Phi(x,y) = -\delta(x,y)$; Corollary 1 implies that

$$\Delta v_i(x) = \int_D -f(y) \cdot \mathbf{1}_{D_i}(y)\Delta_x\Phi(x,y)dv(y) = f(x) \cdot \mathbf{1}_{D_i}(x). \tag{102}$$

So, as we claimed above, the v_i solve the Poisson problem on D_i and vanish everywhere else. If u is a potential solving the connected Poisson problems of Equation (85), then we define

$$w_i(x) := \begin{cases} u - \frac{v_i}{\sigma_i} & \text{if } x \in D_i \\ -\frac{v_i}{\sigma_i} & \text{if } x \notin \mathbb{R}^3 \setminus \overline{D_i} \end{cases}. \tag{103}$$

Recall that we denote the jump of f across the surface S_j as $[f]_j(x) = f_-(x) - f_+(x)$ for $x \in S_j$. Using the fact that u and v_i are continuous throughout $\mathbb{R}^3$, we have that

$$[w_i]_i = \left(u_- - \frac{(v_i)_-}{\sigma_i}\right) + \frac{(v_i)_+}{\sigma_i} = u_- = u, \tag{104}$$

and,

$$[w_i]_{i-1} = -\frac{(v_i)_-}{\sigma_i} - \left(u_+ - \frac{(v_i)_+}{\sigma_i}\right) = u_+ = u. \tag{105}$$

Likewise, using the fact that v_i has a continuous normal derivative throughout $\mathbb{R}^3$, we find:

$$\begin{aligned} [\partial w_i/\partial n]_i &= \frac{\partial u_-}{\partial n}, \text{ and} \\ [\partial w_i/\partial n]_{i-1} &= \frac{\partial u_+}{\partial n}. \end{aligned} \tag{106}$$

Notice that each w_i is harmonic on the domain $\mathbb{R}^3 \setminus \partial D_i$, since on the one hand,

$$\Delta w_i(x) = \Delta u(x) - \frac{\Delta v_i(x)}{\sigma_i} = \frac{f(x)}{\sigma_i} - \frac{f(x) \cdot \mathbf{1}_{D_i}(x)}{\sigma_i} = 0, \text{ for all } x \in D_i, \tag{107}$$

and on the other hand, $\Delta v_i(x) = f(x) \cdot \mathbf{1}_{D_i}(x) = 0$ for $x \in \mathbb{R}^3 \setminus \overline{D_i}$. Hence, we can apply Theorem 13 to express the limiting values of w_i at the surface S_i from both sides in terms of its jumps, which we saw were given by u and its normal derivative. Using also the boundary equation $[\sigma \partial u/\partial n]_i = 0$, one arrives at the symmetric integral equation (cf. Equation (21) in [34]),

$$\begin{aligned} &(\partial v_{i+1}/\partial n) - (\partial v_i/\partial n) \\ &= \sigma_i \mathcal{N}_{S_{i-1}}(u) - (\sigma_i + \sigma_{i+1})\mathcal{N}_{S_i}(u) + \sigma_{i+1}\mathcal{N}_{S_{i+1}}(u) \\ &- \mathcal{D}^*_{S_{i-1}}(p) + 2\mathcal{D}^*_{S_i}(p) - \mathcal{D}^*_{S_{i+1}}(p), \text{ on the surface } S_i, \end{aligned} \tag{108}$$

where $p(x) = \sigma_i[\partial w_i/\partial n]_i(x)$ for every $x \in S_i$, and where $\mathcal{N}_S$ and $\mathcal{D}^*_S$ denote the potentials of Definition 1, where we specify that the domain of integration is taken over the surface S.

Remark 9. The values $(\partial v_{i+1}/\partial n)(x)$ and $(\partial v_i/\partial n)(x)$ for $x \in S_i$ can be obtained by integrating the source term f according to Equation (101). Therefore, Equation 108 involves exactly two unknowns: the values of the potential u, and of the auxiliary function $p(x) = \sigma_i[\partial w_i/\partial n]_i(x)$ at the interface S_i. So, as in the case of the double-layer formulation (Equation (90)), we retrieve the values of u at the interfaces directly.

V. Software and Applications

We conclude this paper with a brief summary of available software and current applications. We distinguish two types of software which rely on boundary element method (BEM) solvers: those which incorporate fast multipole method (FMM) acceleration, and those which do not.

The traditional BEM without FMM acceleration is widely used for exploring, visualizing, and analyzing human neurophysiological data stemming from MEG, EEG, *stereoelectroencephalography* (sEEG) [54], and *electrocorticography* (ECoG) [63], among other techniques. Figure 3 shows some low-resultion BEM models with three head compartments (skin, skull, and brain) which are presently used in BEM computations for M/EEG.

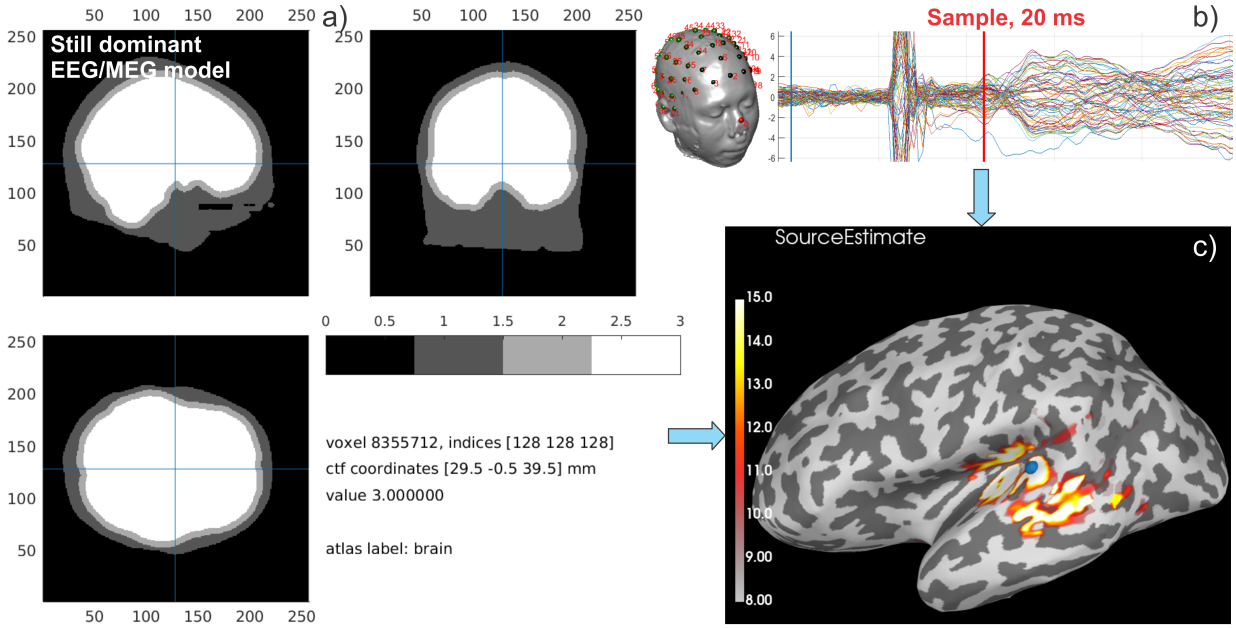


Figure 3: a) BEM for three nested compartments, routinely used in EEG source reconstruction packages [17], [49], [62] (image taken from FieldTrip documentation [13]). b) After the source reconstruction with temporal EEG data from a butterfly plot is done, the result may be projected back onto a detailed white matter surface as shown in c).

Below we list major open-source BEM software packages which are widely used:

- MNE [18] is an academic software package providing a complete data analysis pipeline for M/EEG. It consists of three core subpackages, MNE-C, MNE-MATLAB, and MNE-Python [17]. It computes forward solutions over a spherical head model, or with a nested BEM model of one or three compartments. It provides several functionalities including reading and processing data from different recording systems, forward and inverse modeling, statistical analysis, and machine learning models of neural activity. The package can be used alongside FreeSurfer [11] which creates 3D image segmentations of the head from MRI data.

- Brainstorm [42], [62] is a user-friendly software, with a graphical user interface (GUI) which does not require programming knowledge. It is mainly built on MATLAB scripts, and it implements tools that provide a complete pipeline for analysis

of bioelectric recordings. It incorporates automatic 3D image segmentation of the head via MRI images, and it can integrate information originating from several different sources including cardiac activity, and eye movement. It also includes several data processing tools for M/EEG time series, such as automatic artifact detection. It does not currently incorporate FMM acceleration in its forward solvers, but this is projected to be included in the future.

- FieldTrip [49] is a MATLAB toolbox for M/EEG analysis. It does not incorporate a GUI. It provides functionality to perform source reconstruction from combined MEG and EEG data, as well as analysis of ECoG and sEEG recordings.

- EEGLAB [10] is an interactive MATLAB toolbox for processing E/MEG data. It can incorporate independent component analysis (ICA) [29] into the source-localization problem. ICA is a statistical method in signal processing, designed to recover the components of a linear superposition of signals, given its projection on several sensors. In the EEG problem these sensors are the scalp electrodes. The ICA step can be useful in detecting different types of EEG signals, such as those originating from seizure-related activity.

- OpenMEEG [19] implements a high-accuracy solver using the symmetric boundary element method of Kybic et. al. [34]. It can be called using MATLAB from Brainstorm or Fieldtrip, and can also be used as a Python module.

- The Helisnki BEM Framework (HBF) [58], [59] is a MATLAB library implementing a BEM solver using the *isolated source approach* (ISA) [26], [60]. This approach was introduced to handle numerical difficulties arising from the low relative conductivity of the skull, and it is obtained by splitting the potential into two components, one of which assumes that the skull is a perfect insulator.

To the date of writing, the packages above do not incorporate FMM acceleration. The traditional BEM cannot handle models with more than approximately 50,000 facets on the surfaces, and because of this the brain shell structures need to be simplified and downsampled.

On the other hand, the FMM-accelerated algorithms can process human head models of up to 60–70 million facets, including fine details such as the three brain meninges [66]. Currently, the FMM-accelerated software is mainly used for fast TMS and DBS computations [9], [40], and for the neuronal arbor modeling at microscale [46]. Typical simulation results can be found in [38]. An open-source implementation of FMM-accelerated BEM software, in the form of MATLAB-based scripts, can be found in the TMSCoreLab Github site [64], which includes applications to M/EEG, TMS, and TES. Figure 4 shows simulation results of a TMS application on different interfaces of a detailed brain model taken from the *Human Connectome Project* (HPC) [65]. Note that skin, skull and cerebrospinal fluid shells are in fact present in the model, but removed from visualization for clarity.

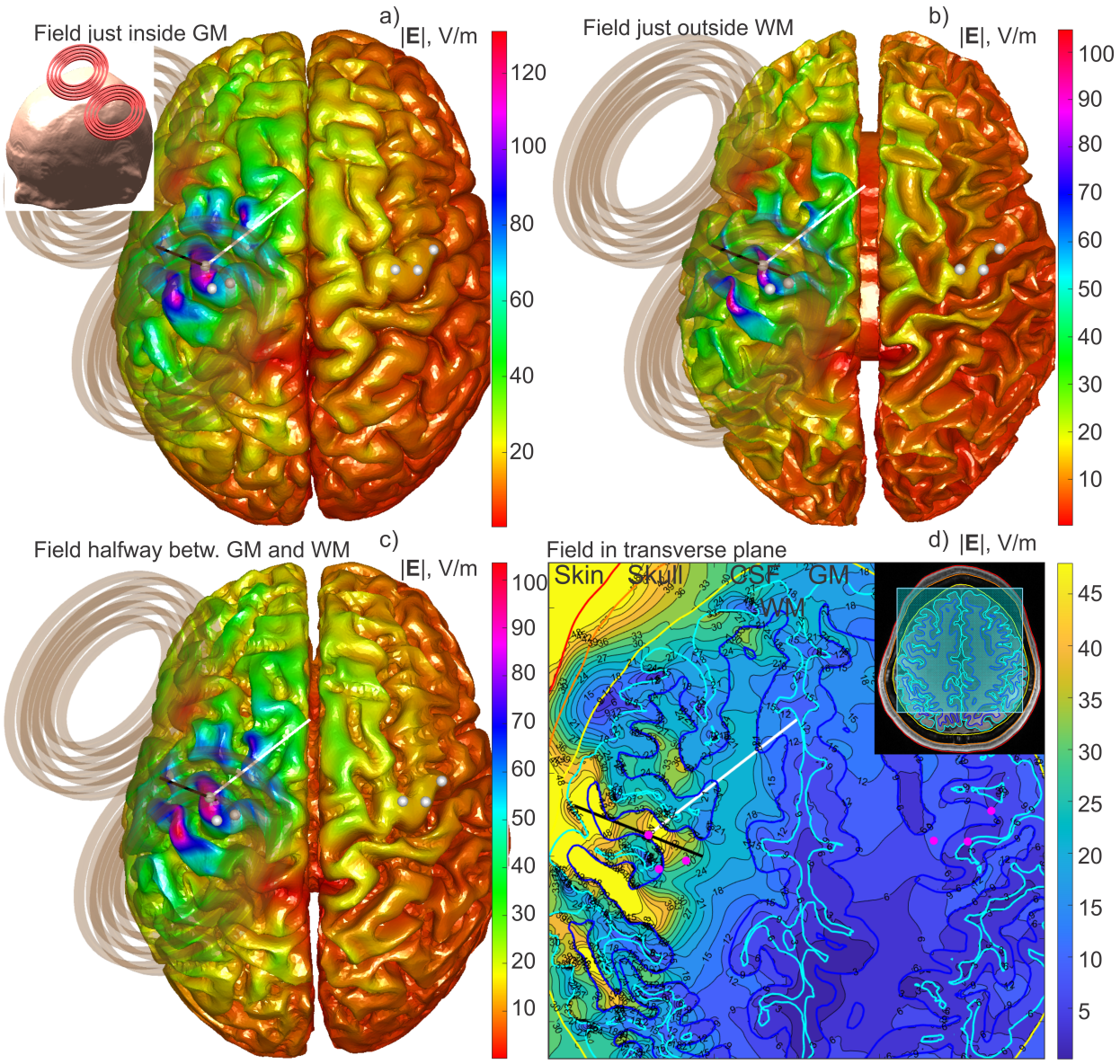


Figure 4: Different images of an FMM-accelerated simulation output for HPC subject 120111 [65] (image taken from [38]). The model has a total of 1 million facets. a) Total electric field just inside of the gray matter interface; b) Total electric field just outside the white matter interface; c) Total electric field at the cortical midsurface; d) Total electric field in a transverse plane beneath the coil. The entire computational sequence runs in approximately 4.7 s including graphical rendering in MATLAB.

Conclusions

We surveyed the main examples of integral equations used in bioelectric modeling, and illustrated how the surface charge density equations and the surface potential equations are dual to each other via a modification of Geselowitz's formula. The jump relations of the potential theory, together with Green's formula and its generalization due to Smythe, constitute the main theoretical tools that have been used in the subject. We clarified many of the details that typically are glanced over on most expositions. We reviewed the major software packages for bioelectric modeling that are currently available, and noted how FMM acceleration of the algorithms enables us to deploy more realistic models, and carry faster computations.

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