A COMPUTATIONAL APPROACH FOR THE INVERSE PROBLEM OF NEURONAL CONDUCTANCES DETERMINATION

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Abstract. The derivation by Alan Hodgkin and Andrew Huxley of their famous neuronal conductance model relied on experimental data gathered using neurons of the giant squid. It becomes clear that determining experimentally the conductances of neurons is hard, in particular under the presence of spatial and temporal heterogeneities. Moreover it is reasonable to expect variations between species or even between types of neurons of a same species. Determining conductances from one type of neuron is no guarantee that it works across the board.

We tackle the inverse problem of determining, given voltage data, conductances with non-uniform distribution computationally. In the simpler setting of a cable equation, we consider the Landweber iteration, a computational technique used to identify non-uniform spatial and temporal ionic distributions, both in a single branch or in a tree. Here, we propose and (numerically) investigate an iterative scheme that consists in numerically solving two partial differential equations in each step. We provide several numerical results showing that the method is able to capture the correct conductances given information on the voltages, even for noisy data.

1. Introduction.

The seminal model of Hodgkin and Huxley \cite{Hodgkin1952} of neuronal voltage conductance describes how action potential occurs and propagate. It is a landmark model, and present an outstanding combination of modeling based on physical arguments and experimental data, needed to determine the behavior of ion channels. Our Holy Grail is to determine such behavior as well, but directly from voltage measurements, not relying on excruciating data fitting.

Finding the conductances is crucial of one want to emulate the neuronal voltage propagation using computational models, since the conductances are part of the data requires by the models. Mimicking the work of Hodgkin and Huxley for every single neuron and or experimental condition is unfeasible. What we offer is a computational way to determine the conductances based on experimental data that is readily available to the researcher.

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Our method can also be extended to several computational models, such as the FitzHugh-Nagumo, Morris-Lecar, Hodgkin-Huxley, etc.

We use a simplified neuronal model, the cable equation \[3, 17, 37\], given by a parabolic partial differential equation. We consider first the case of a single branch of length \(L\), represented by the interval \([0, L]\). The more general case of a branched tree is described in the Section 2.3. In the cable model the membrane electrical potential \(V : [0, T] \times [0, L] \rightarrow \mathbb{R}\) solves

\[
C_M \frac{\partial V}{\partial t} = \frac{1}{R_I + R_E} \frac{\partial^2 V}{\partial x^2} + I_{\text{ion}} \quad \text{in} \ (0, T) \times (0, L),
\]

where \(R_I, R_E\) are the internal and external neuronal resistance; \(C_M\) represents the membrane capacitance per unit area. For the passive cable models, the ionic current is given by

\[
I_{\text{ion}}(t, x) = \sum_{i \in \text{Ion}} G_i(t, x)(V(t, x) - E_i),
\]

where Ion is the set of ions being considered in the modeling, for example, Ion = \{K, Na, Leak\}. Also, \(G_i(t, x)\) is the conductance for each ion \(i \in \text{Ion}\), and it might depend on spatial and temporal variables, as indicated in the notation. In this paper, these functions are not known. Finally, \(E_i\) is the Nernst potential for each ion \(i \in \text{Ion}\).

To equation (1) we add boundary and initial conditions given by

\[
\frac{\partial V}{\partial x}(t, 0) = p(t), \quad \frac{\partial V}{\partial x}(t, L) = q(t), \quad V(0, x) = r(x),
\]

We assume that the constants \(C_M, R_I, R_E\) and \(E_i\), and the functions \(p, q\) and \(r\) are given data.

Let \(c = C_M(R_I + R_E)\) be positive, and \(g_i(t, x) = G_i(t, x)(R_I + R_E)\). We gather then from (1) and (2) that

\[
\begin{align*}
V_{xx}(t, x) &= cV_t(t, x) + \sum_{i \in \text{Ion}} g_i(t, x)[V(t, x) - E_i], \\
V(0, x) &= r(x), \quad x \in [0, L], \\
V_x(t, 0) &= p(t), \quad V_x(t, L) = q(t) \quad t \in [0, T],
\end{align*}
\]

The inverse problem of finding “correct” conductances \(g_i\) given some measurements of the voltage is “hard”, in the sense that it leads to ill-posed problems \[40\], and that might explains why the vast majority of related research avoids the problem of finding spatially dependent parameters. There are several approaches to deal with the problem in hand, but certainly no panacea.

Hodgkin and Huxley \[20\] tackled such problem by data fitting. Wilfrid Rall and co-authors considered several related questions for the cable equation \[31, 32, 33, 34, 35, 21\].
See also [38, 22, 6, 15, 14, 36, 25]. In [41], there is an interesting attempt to introduce heterogeneity into the Hodgkin and Huxley model.

We consider next references with a stronger mathematical flavor; see however [42] for a biologically inclined work where the authors consider the branched cable equation with the chemical synapses, and convert somatic conductances to dendritic conductances.

Uniqueness of solutions for finding constant parameters in the cable equation, and related methods, are considered in [8, 11, 13], and [10] for a nonlinear model; see also [1, 30] for further considerations related to existence and uniqueness. In [12] a more involved problem was tackled based on the FitzHugh–Nagumo and Morris–Lecar models, and where nonlinear functions modeling the conductances are sought. The method is based on fixed point arguments, and despite its ingenuity, it is not clear how to extend it to more involved models or to accommodate for spatially distributed ions channels.

In [4, 39, 9, 1, 2], the question of determining spatially distributed conductances is investigated through different techniques and algorithms. They differ considerably from our method, and seem harder to generalize for other situations, as, for instance, when the domain is given by trees (with the obvious exception of [1, 2]), for time dependent conductances, and for general nonlinear equations, our ultimate goal.

Inverse problems are ill-posed, and, under certain conditions, the Landweber method provides convergent iterative scheme. The main goal of the present paper is to develop the Nonlinear Landweber method to solve the inverse problem of recovering the conductances in the cable equation. We also test the scheme under different scenarios.

We next outline the contents of the paper. In Section 2, we present the Landweber method, detailing how it should be applied in the cases of a non-branched and branched cable, where the geometry is given by a tree. In Section 3, we present the related numerical results. In Section 4, we present some concluding remarks, and in the Appendix we describe an abstract formulation of the Landweber method.

2. The Landweber Method Applied to the Conductance Determination

We describe the abstract form of the Landweber method in the Appendix. Here we consider its application to the problem at hand, that is, knowing the voltage $V$ at the space-time domain $\Gamma$, we want to determine $g_i$, assuming that (3) holds. We consider three different cases, depending on where the voltage is known. In the first case, we assume that $V$ is known at all points, i.e., $\Gamma = [0, T] \times [0, L]$. In the remaining cases, we assume that the voltage is known at both or only one end points, and all times. Thus $\Gamma = [0, T] \times \{0, L\}$ or $\Gamma = [0, T] \times \{L\}$. This is summarized in Table 1, along with other definitions.
Let $\Omega = [0,T] \times [0,L]$, $N_{\text{ion}}$ the number of ions of the set $\text{Ion}$, and the vector $\mathbf{g} = (g_1, \ldots, g_{N_{\text{ion}}})$. In this article we work with the functional Hilbert space of square integrable functions $L^2(\Omega)$, and the Banach space of “essentially” bounded functions $L^\infty(\Omega)$ (see [27] for precise definitions). Given $f \in L^2(\Omega)$ and $g$ continuous and bounded in $\Omega$, we define the norms

$$
\|f\|^2_{L^2(\Omega)} = \int_\Omega |f(\xi)|^2 \, d\xi, \quad \|g\|^2_{L^\infty(\Omega)} = \sup_{\xi \in \Omega} |g(\xi)|,
$$

where $\sup$ stands for supremum.

Consider the nonlinear operator

$$
F : D(F) \to R(F)
$$

defined by $F(\mathbf{g}) = V|_\Gamma$, where $V$ solves (3) and $D(F) = (L^\infty(\Omega))^{N_{\text{ion}}}$. Also $R(F)$ and $V|_\Gamma$ are defined as in Table 1.

We consider the inverse problem of finding an approximation for $\mathbf{g}$, given the noisy data $V^\delta|_\Gamma$, where

$$
\|V - V^\delta\|_{L^\infty(\Omega)} \leq \delta,
$$

for some known noise threshold $\delta > 0$. That makes sense since in practice, the data $V|_\Gamma$ are never known exactly, and it is why we work with the data actually obtained $V^\delta|_\Gamma$, within a certain given precision $\delta > 0$. In section 3 we detail the type of noise introduced.

Define in $R(F)$ the inner product

$$
\langle V^\delta|_\Gamma - V^k, W^k|_\Gamma \rangle_{R(F)} = \alpha_1 \int_0^L \int_0^T (V^\delta(t, x) - V^k(t, x)) W^k(t, x) \, dt \, dx
$$

$$
- \alpha_2 \int_0^T (V^\delta(t, 0) - V^k(t, 0)) W^k(t, 0) \, dt + \alpha_3 \int_0^T (V^\delta(t, L) - V^k(t, L)) W^k(t, L) \, dt,
$$

where $\alpha_1$, $\alpha_2$ and $\alpha_3$ are as in Table 1.

| CASE I | CASE II | CASE III |
|--------|---------|---------|
| $\Gamma = [0,T] \times [0,L]$ | $\Gamma = [0,T] \times [0,L]$ | $\Gamma = [0,T] \times \{L\}$ |
| $R(F) = L^2([0,T] \times [0,L])$ | $R(F) = [L^2[0,T]]^2$ | $R(F) = L^2[0,T]$ |
| $V|_\Gamma = V(\cdot, \cdot)$ | $V|_\Gamma = (-V(\cdot, 0), V(\cdot, L))$ | $V|_\Gamma = V(\cdot, L)$ |
| $W|_\Gamma = W(\cdot, \cdot)$ | $W|_\Gamma = (-W(\cdot, 0), W(\cdot, L))$ | $W|_\Gamma = W(\cdot, L)$ |
| $\alpha_1 = 1; \alpha_2 = 0; \alpha_3 = 0$ | $\alpha_1 = 0; \alpha_2 = -1; \alpha_3 = 1$ | $\alpha_1 = 0; \alpha_2 = 0; \alpha_3 = 1$ |

Table 1. Summary of the three different cases considered in this paper. We seek the conductances $g_i$ assuming that (3) holds and that the voltage $V$ is known at the space-time domain $\Gamma$ defined above along with other definitions.
Given the initial guess \( g^{1,\delta} \in (L^\infty(\Omega))^{N_{\text{ion}}} \), the Landweber approximation for \( g \) is defined by the sequence

\[
g^{k+1,\delta} = g^{k,\delta} + F'(g^{k,\delta})^*(V^\delta|_\Gamma - F(g^{k,\delta})) \quad \text{for} \ k \in \mathbb{N}.
\]

As stopping criteria we use the \textit{discrepancy principle} with \( \tau > 2 \) (See [23]), i.e.,

\[
\|V^\delta|_\Gamma - F(g^{k,\delta})\|_{R(F)} \leq \tau \delta \leq \|V^\delta|_\Gamma - F(g^{k,\delta})\|_{R(F)},
\]

for all \( 0 \leq k < k_* \). We next compute the Gâteaux derivative \( F' \) and its adjoint \( F'(^*\cdot) \).

2.1. \textbf{The adjoint operator} \( F'(^*\cdot) \). Given \( g^{k,\delta} \in D(F) \) and the vector \( \theta = (\theta_1, \ldots, \theta_{N_{\text{ion}}}) \), the Gâteaux derivative of \( F \) at \( g^{k,\delta} \) in the direction \( \theta \in (L^\infty(\Omega))^{N_{\text{ion}}} \) is given by

\[
F'(g^{k,\delta})(\theta) = \lim_{\lambda \to 0} \frac{F(g^{k,\delta} + \lambda \theta) - F(g^{k,\delta})}{\lambda} = W^k|_\Gamma,
\]

where \( W^k \) solves

\[
W^k_{xx}(t, x) - cW^k_t(t, x) - \sum_{i \in \text{Ion}} g_i^{k,\delta}(t, x)W^k(t, x) = \sum_{i \in \text{Ion}} \alpha_i (V^k(t, x) - E_i) \quad \text{in} \ \Omega,
\]

\[
W^k(0, x) = 0 \quad \text{for} \ x \in [0, L], \quad W^k_x(t, 0) = W^k_x(t, L) = 0 \quad \text{for} \ t \in [0, T],
\]

and \( V^{k,\delta} \) solves (3) with \( g_i \) replaced by \( g_i^{k,\delta} \). To obtain (9) from (8), it is enough to consider the difference between problem (3) with coefficients \( g^{k,\delta} + \lambda \theta \) and \( g^{k,\delta} \), divide by \( \lambda \) and take the limit \( \lambda \to 0 \).

Consider now the following PDE with \textit{final condition}:

\[
\begin{align*}
-U^k_{xx}(t, x) - cU^k_t(t, x) + \sum_{i \in \text{Ion}} g_i^{k,\delta}(t, x)U^k(t, x) &= \alpha_1 (V^\delta(t, x) - V^{k,\delta}(t, x)), \\
U^k(T, x) &= 0, \quad x \in [0, L], \\
U^k_x(t, 0) &= \alpha_2 (V^\delta(t, 0) - V^{k,\delta}(t, 0)), \quad t \in [0, T], \\
U^k_x(t, L) &= \alpha_3 (V^\delta(t, L) - V^{k,\delta}(t, L)), \quad t \in [0, T].
\end{align*}
\]

The variables \( \alpha_1, \alpha_2 \) and \( \alpha_3 \) are defined in Table 1. Let \( V^{k,\delta}|_\Gamma = F(g^{k,\delta}) \). From the Landweber iteration (6), we gather that

\[
\langle g^{k+1,\delta} - g^{k,\delta}, \theta \rangle_{(L^2(\Omega))^{N_{\text{ion}}}} = \langle F'(g^{k,\delta})^*(V^\delta|_\Gamma - F(g^{k,\delta})), \theta \rangle_{(L^2(\Omega))^{N_{\text{ion}}}}
\]

\[
= \langle F'(g^{k,\delta})^*(V^\delta|_\Gamma - V^{k,\delta}|_\Gamma), \theta \rangle_{(L^2(\Omega))^{N_{\text{ion}}}} = \langle V^\delta|_\Gamma - V^{k,\delta}|_\Gamma, F'(g^{k,\delta}) \cdot \theta \rangle_{R(F)}
\]

\[
= \langle V^\delta|_\Gamma - V^{k,\delta}|_\Gamma, W^k|_\Gamma \rangle_{R(F)}.
\]

Although (11) yields an interesting relation, it carries an impeding dependence on \( \theta \) through \( W^k \). It is possible to avoid that by performing some “trick” manipulations. Multiplying the
that the first equation of (10) by $-W^k$, and integrating in the intervals $[0, T]$ and $[0, L]$ we gather that

$$
\int_0^L \int_0^T U_{xx}^k(t, x) W^k(t, x) \, dt \, dx + \int_0^L \int_0^T c \, U_t^k(t, x) W^k(t, x) \, dt \, dx
$$

$$
- \int_0^L \int_0^T \sum_{i \in \text{ion}} f_{i}^{k, \delta}(t, x) U^k(t, x) W^k(t, x) \, dt \, dx =
$$

$$
- \alpha_1 \int_0^L \int_0^T (V^\delta(t, x) - V^{k, \delta}(t, x)) W^k(t, x) \, dt \, dx.
$$

Integrating for parts the first term of (12) with respect to the space variable twice, and using the boundary conditions for $W^k$ we have

$$
\int_0^L \int_0^T U_{xx}^k(t, x) W^k(t, x) \, dt \, dx = \int_0^L \int_0^T U^k(t, x) W_{xx}^k(t, x) \, dt \, dx + \int_0^L U_x^k(t, x) W^k(t, x)|_0^L \, dt,
$$

where we denote $U_{xx}^k(t, x) W^k(t, x)|_0^L = U^k(t, L) W^k(t, L) - U^k(t, 0) W^k(t, 0)$. Similarly, integrating for parts the second term of (12) with respect to time and using the initial condition of $W^k$ and the final condition of $U^k$, we gather that

$$
\int_0^L \int_0^T \left( W_{xx}^k(t, x) - c U_t^k(t, x) - \sum_{i \in \text{ion}} g_{i}^{k, \delta}(t, x) \right) U^k(t, x) \, dt \, dx =
$$

$$
- \alpha_1 \int_0^L \int_0^T \left( V^\delta(t, x) - V^{k, \delta}(t, x) \right) W^k(t, x) \, dt \, dx - \int_0^L U_x^k(t, x) W^k(t, x)|_0^L \, dt.
$$

Substituting (13) and (14) in (12), it follows that

$$
\int_0^L \int_0^T \left( W_{xx}^k(t, x) - c U_t^k(t, x) - \sum_{i \in \text{ion}} g_{i}^{k, \delta}(t, x) \right) U^k(t, x) \, dt \, dx =
$$

$$
- \alpha_1 \int_0^L \int_0^T \left( V^\delta(t, x) - V^{k, \delta}(t, x) \right) W^k(t, x) \, dt \, dx - \int_0^L U_x^k(t, x) W^k(t, x)|_0^L \, dt.
$$

Substituting the first equation of (9) in the previous equation, we obtain

$$
\int_0^L \int_0^T \sum_{i \in \text{ion}} \theta_i (V^{k, \delta}(t, x) - E_i) U^k(t, x) \, dt \, dx = -\alpha_1 \int_0^L \int_0^T \left( V^\delta(t, x) - V^{k, \delta}(t, x) \right) W^k(t, x) \, dt \, dx
$$

$$
- \int_0^L U_x^k(t, x) W^k(t, x)|_0^L \, dt.
$$

From the boundary conditions of (10), the following expression holds

$$
\int_0^L \int_0^T \sum_{i \in \text{ion}} \theta_i (V^{k, \delta}(t, x) - E_i) U^k(t, x) \, dt \, dx = -\alpha_1 \int_0^L \int_0^T \left( V^\delta(t, x) - V^{k, \delta}(t, x) \right) W^k(t, x) \, dt \, dx
$$

$$
+ \alpha_2 \int_0^T \left( V^\delta(t, 0) - V^{k, \delta}(t, 0) \right) W^k(t, 0) \, dt - \alpha_3 \int_0^T \left( V^\delta(t, L) - V^{k, \delta}(t, L) \right) W^k(t, L) \, dt.
$$
From the previous equation and the definition of the inner product (5), we have
\begin{equation}
\int_0^L \int_0^T \sum_{i \in \text{Ion}} \theta_i (V^{k,\delta}(t,x) - E_i) U^k(t,x) \, dt \, dx = - \langle V^\delta |_{\Gamma} - V^{k,\delta} |_{\Gamma}, W^k |_{\Gamma} \rangle_{R(F)}.
\end{equation}
From (11) and (15) we have
\begin{equation}
\int_0^L \int_0^T \sum_{i \in \text{Ion}} \theta_i \left( g^{k+1,\delta}_i(t,x) - g^{k,\delta}_i(t,x) \right) \, dt \, dx = - \int_0^L \int_0^T \sum_{i \in \text{Ion}} \theta_i (V^{k,\delta}(t,x) - E_i) U^k(t,x) \, dt \, dx.
\end{equation}
Since $\theta \in (L^2(\Omega))^{N_{\text{Ion}}}$ is arbitrary, we gather that the following iteration holds:
\begin{equation}
g^{k+1,\delta}_i(t,x) = g^{k,\delta}_i(t,x) - (V^{k,\delta}(t,x) - E_i) U^k(t,x) \quad \text{for all } i \in \text{Ion}
\end{equation}
\begin{remark}
Note from (16) that $g^{k+1,\delta}_i(T,x) = g^{k,\delta}_i(T,x)$ for all $x \in [0,L]$ and every $k \in \mathbb{N}$, since, from (10), $U^k(T,x) = 0$. Thus, $g^{k,\delta}_i$ is never corrected at final time $T$. To recover $g_i$ at time $T$, we consider multiple experiments (Landweber-Kaczmarz method \cite{23}), one forward and another backward in time. The derivations for the backward in time case are the same as above, except that we change the signal of the derivatives with respect to time in the PDEs (3) and (10). We also change the following conditions: $V(0,x) = r(x)$ by $V(T,x) = r(x)$ and $U^k(T,x) = 0$ by $U^k(0,x) = 0$. We detail such changes in Section 2.2.
\end{remark}
In the case of a single experiment, the numerical scheme would be as follows. Check Table 1 for notation.
\begin{itemize}
\item Data: $V^\delta |_{\Gamma}$, $r$, $p$, $q$, $\delta$, $\tau$
\item Result: Compute an approximation for $g$ using Landweber Iteration Scheme
\end{itemize}
Choose $g^{1,\delta}$ as an initial approximation for $g$;
Compute $V^{1,\delta} |_{\Gamma}$ from (3) by replacing $g$ by $g^{1,\delta}$;
\begin{verbatim}
k=1;
while $\tau \delta \leq \|V^\delta |_{\Gamma} - V^{k,\delta} |_{\Gamma}\|_{R(F)}$ do
    Compute $U^k$ from (10);
    Compute $g^{k+1,\delta}$ using (16);
    Compute $V^{k+1,\delta}$ from (3), replacing $g$ by $g^{k+1,\delta}$;
    $k \leftarrow k + 1$;
end
\end{verbatim}
\begin{algorithm}
Algorithm 1: Nonlinear Landweber Iteration
\end{algorithm}
\begin{remark}
Whenever $g$ is time independent, and in this case we write $g(t,x) = g(x)$, the interaction is defined by
\begin{equation}
g^{k+1,\delta}_i = g^{k,\delta}_i - \frac{1}{T} \int_0^T (V^{k,\delta} - E_i) U^k \, dt \quad \text{for } i \in \text{Ion}.
\end{equation}
\end{remark}
Remark 3. Note that the numerical solutions of two PDEs are needed for each iteration. Of course, the solutions are obtained numerically, and for that we use finite difference scheme in space coupled with backward Euler in time. To compute the integral in (17) we use the trapezoidal rule. In what follows we assume that the numerical approximations are accurate enough. All the experiments performed using Matlab®.

2.2. Multiple experiments. It might be convenient to have data from multiple experiments to guarantee a better approximation for the conductivities. In this case, a simple modification of the Algorithm 1 is necessary [23]. In our case, such multiple experimental approach is also necessary, as noted in Remark 1. We detail here the necessary changes.

So assume we have two experiments yielding the data \( V_\delta|_{\Gamma}^{F} \) and \( V_\delta|_{\Gamma}^{B} \) (the letter “F” stands for forward and “B” for backward). Assume that the first experiment yields \( V_\delta|_{\Gamma}^{F} \), and obeys (3) with \( r = r_F, p = p_F \) and \( q = q_F \) given. Assume that the second experiment yields \( V_\delta|_{\Gamma}^{B} \) and follows a similar equation, but backwards in time. By performing the change of variables \( t \rightarrow T - t \), we gather that the same equation holds, but now with

\[
\begin{aligned}
V_{xx}(t,x) &= c V_t(t,x) + \sum_{i \in I_0} g_i(T - t, x)[V(t,x) - E_i], \\
V(0, x) &= r_B(x), \quad x \in [0, L], \\
V_x(t,0) &= p_B(T - t), \quad V_x(t,L) = q_B(T - t) \quad t \in [0, T].
\end{aligned}
\]

The actual solution is \( V_B(t,x) = V(T - t, x) \).

We also define the backward in time equation equivalent of (10) (with final condition), and again perform the change of variables \( T - t \), yielding

\[
\begin{aligned}
- U_{xx}^k(t,x) + c U_t^k(t,x) + \sum_{i \in I_0} g_i^{k,\delta}(T - t, x) U^k(t,x) &= \alpha_1 \left( V_B^\delta(T - t, x) - V_{B}^{k,\delta}(T - t, x) \right), \\
U^k(0, x) &= 0, \quad x \in [0, L], \\
U_x^k(t,0) &= \alpha_2 \left( V_B^\delta(T - t, 0) - V_{B}^{k,\delta}(T - t, 0) \right), \quad t \in [0, T], \\
U_x^k(t,L) &= \alpha_3 \left( V_B^\delta(T - t, L) - V_{B}^{k,\delta}(T - t, L) \right), \quad t \in [0, T].
\end{aligned}
\]

The actual solution is \( U_B^k = U_k \). Again, the variables \( \alpha_1, \alpha_2 \) and \( \alpha_3 \) are as in Table 1.
In terms of the algorithm, we gather the following.

**Data:** $V_F^δ|_Γ$, $V_B^δ|_Γ$, $r_F$, $r_B$, $p_F$, $p_B$, $q_F$, $q_B$, $δ$, $τ$

**Result:** Compute an approximation for $g$ using Landweber Iteration Scheme

Choose $g^{1,δ}$ as an initial approximation for $g$;

Compute $V_F^{1,δ}|_Γ$ from [3] by replacing $g$ by $g^{1,δ}$ and $r$, $p$, $q$ by $r_F$, $p_F$, $q_F$;

Compute $V_B^{1,δ}|_Γ$ from [18] by replacing $g$ by $g^{1,δ}$;

$k=1$;

while $2τ^2δ^2 ≤ ∥V^δ_Γ − V^{k,δ}_F∥^2_{R(Γ)} + ∥V^δ_Γ − V^{k,δ}_B∥^2_{R(Γ)}$ do

Compute $U^k_F$ from [10], given $g^{k,δ}$;

Compute $g^{k+1,δ}$ using [16], replacing $V^{k,δ}$ by $V^{k,δ}_F$ and $U^k$ by $U^k_F$;

Compute $U^k_B$ from [19], replacing $g^k$ by $g^{k+1,δ}$;

Compute $V^{k+1}_B$ from [18], replacing $g$ by $g^{k+1,δ}$;

Compute $g^{k+1,δ}$ using [16], replacing $V^{k,δ}$ by $V^{k+1,δ}_B$ and $U^k$ by $U^{k+1}_B$;

Compute $V^{k+1}_F$ from [18], replacing $g$ by $g^{k+1,δ}$;

$k ← k + 1$;

end

**Algorithm 2:** Nonlinear Landweber Iteration for two experiments

A parallel version of the above algorithm is obtained by updating $g$ simultaneously. Also, the modification to accommodate several experiments is trivial.

2.3. The Landweber Method applied to the conductance determination defined on a tree. Following the notation of [1, 2], we let $Θ = E \cup V$ be a tree, where $E = \{e_1, e_2, \cdots, e_r\}$ is a set of edges, $V = \{ν_1, ν_2, \cdots, ν_M\}$ is a set of vertices, and the edges are connected at the vertices $ν_j$. Let $\{γ_1, γ_2, \cdots, γ_m\} = ∂Θ ⊂ V$, i.e. if the index of a vertex, $id(ν)$, is the number of edges incident to it, then $∂Θ = \{ν ∈ V : id(ν) = 1\}$. Hence $V \setminus ∂Θ = \{ν ∈ V : id(ν) > 2\}$. In Figure 1 we depict a simple example of a tree with one bifurcation point.

Our cable equation model defined on a tree is given by

\[
\begin{align*}
V_{xx}(t, x) &= cV_t(t, x) + \sum_{i \in Ion} g_i(t, x) [V(t, x) − E_i], \quad \text{in } (0, T) \times E, \\
V(0, x) &= r(x), \quad \text{in } x ∈ Θ, \\
V_x(t, γ_k) &= f_k(t), \quad \text{at each vertex } γ_k ∈ ∂Θ \text{ and } t ∈ [0, T], \\
\sum_{e_j \sim ν} V'_j(t, ν) &= 0, \quad \text{at each vertex } ν ∈ V \setminus ∂Θ \text{ and } t ∈ [0, T],
\end{align*}
\]

where $c$, $r$, $f_k$ and $g = (g_1, \ldots, g_{N_{ion}})$ are the given data; cf [3].
The last equation, of the EDP \((20)\), \(V_j'(\nu)\) denotes the derivative of \(V\) at the vertex \(\nu\) taken along the edge \(e_j\) in the direction towards the vertex. Also, \(e_j \sim \nu\) means edge \(e_j\) is incident to vertex \(\nu\), and the sum is taken over all edges incident to \(\nu\). Since \(\partial \Theta\) consists of \(m\) vertices, \(f_k\) can be naturally identified with a function acting from \([0, T]\) to \(\mathbb{R}^m\).

Let \(\Omega = (0, T) \times \Theta\) and define the operator

\[
F : L^2(\Omega) \to L^2(\Omega)
\]

such that \(F(g) = V(\cdot, \cdot)\), where \(V\) solves \((20)\). The objective of this section is to, given \(V^\delta\), obtain an approximation to \(g\), using the method \((6)\). To compute the adjoint operator \(F'(\cdot)^*\), we define the following PDE:

\[
\begin{align*}
- U_{xx}^k(t, x) - c U_t^k(t, x) + \sum_{i \in I_\Theta} g_i(t, x) U^k(t, x) &= V^\delta(t, x) - V^{k, \delta}(t, x), \quad \text{in } (0, T) \times \mathcal{E}, \\
U^k(T, x) &= 0, \quad \text{in } x \in \Theta, \\
U_x^k(t, \gamma_k) &= 0, \quad \text{at each vertex } \gamma_k \in \partial \Theta \text{ and } t \in [0, T], \\
\sum_{e_j \sim \nu} U_{j}^l(t, \nu) &= 0, \quad \text{at each vertex } \nu \in V \setminus \partial \Theta \text{ and } t \in [0, T].
\end{align*}
\]

By doing the same procedure as subsection \(2.1\) we obtain \((16)\). Remarks \(1, 2\) and \(3\) also hold in this problem.

### 3. Numerical Simulation

To design our numerical experiments, we first choose \(g\) and compute \(V\) from \((3)\), obtaining then \(V|_\Gamma\). Of course, in practice, the values of \(V|_\Gamma\) are given by some experimental measures, and thus subject to experimental/measurement errors. In our examples, \(V^\delta|_\Gamma\) is obtained by

\[
V^\delta(t, x) = V(t, x) + \text{rand}_{\delta}, \quad \text{for all } (t, x) \in \Gamma
\]
where \( r \) is a uniformly distributed random variable taking values in the range \([-\delta, \delta]\).

Next, given the initial guess \( g^{1,\delta} \) and the data \( V^{\delta}|_{\Gamma} \) and \( \delta \), we start to recover \( g \) using the Algorithm 1. Note that unlike in PDE problems where the exact solution usually has to be computed by numerical over-kill, here we have the exact \( g \), and we use that to gauge the algorithm performance. We denote the following terms

\[
\text{Res}_{k^*} = \|V^{\delta}|_{\Gamma} - F(g^{k^*,\delta})\|_{\mathcal{R}(F)}, \quad \text{Error}_{k^*} = \frac{1}{N_{\text{ion}} \sum_{i \in \text{Ion}}} \frac{\|g_i - g_i^{k^*,\delta}\|_{L^\infty(\Omega)}}{\|g_i\|_{L^\infty(\Omega)}} \times 100\%.
\]

In this section we will present three numerical simulations. The first example considers only an ion (\( \text{Ion} = \{ \text{K} \} \)), with the conductance \( (g = g_{\text{K}}) \) dependent only the spatial variable. In the second example, still with one ion (\( \text{Ion} = \{ \text{K} \} \)), the conductance depends on the spatial and temporal variable. Finally, in the third example, we consider two ions (\( \text{Ion} = \{ \text{K, Na} \} \)), where the conductance \( (g = (g_{\text{K}}, g_{\text{Na}})) \) depends only on the spatial variable. In each example we consider two different values of \( \tau \), based on experimental and theoretical considerations.

**Example 3.1.** We first consider a test problem as in Example 1, which is a particular case of (3) where \( N_{\text{ion}} = 1, E_{\text{K}} = 0, L = 1, c = 1, T = 1, g(t, x) = g_{\text{K}}(x) \) and

\[
r(x) = \cos(x) \sin(0.5 \tan(x)), \quad p(t) = 0.5 \exp(-t), \quad q(t) = 0.068 \exp(-t).
\]

The goal in this numerical test is to find \( g_{\text{K}}(x) = -0.25 \sec^4(x) \) given the boundary condition

\[
V^{\delta}|_{\Gamma} = (-V^{\delta}(-,0), V^{\delta}(\cdot,L)).
\]

Here we introduce perturbation on the boundary data, according to (22). Thus, given \( g_{\text{Na}} \), we compute \( V^{\delta}(\cdot,0) \) and \( V^{\delta}(\cdot,1) \) according to (3) and (22). In this tests we consider the initial guess \( g_{\text{K}}^{1,\delta}(x) = 2x \). We partition the time variable in 30 points and the spatial variable in 20 points. In our experiments we test two different values of \( \tau \) (2.01 and 4), showing its influence.

Table 2 presents the results for various levels of noise. When \( \delta \) decreases, the number of iterations grow resulting in a better approximation for \( g_{\text{K}} \) and smaller residuals. As expected, the results of the fourth and seventh columns are close to \( \tau \delta \), related to the stopping criteria [7].

In Figure 2, we plot some results for \( \delta = 0.02 \). On the left, we plot the initial guess \( g^{1,\delta} \) and the corresponding approximate solutions for \( \tau = 2.01 \) and \( \tau = 4 \). On the right we present the actual error and the residual as a function of the iteration (log plot). Figure 3 displays \( V \) and \( V^{\delta} \).

**Example 3.2.** In this example we used multiple experiments (3) and (18). For the first experiment (3) the initial condition is \( r_F(x) = \sin(x) \) we assume that we know \( V_F^{\delta} \). For the
Table 2. Numerical results for Example 3.1. The first column describes the noise level \( \delta \), as in (22). From the second to the fourth column we present results for \( \tau = 2.01 \), where the second column contains the number of iterations according to (7), and the third column contains the error according to (23). The fourth column presents the residual as in (23). We repeat the same information from the fifth to the seventh column, this time with \( \tau = 4 \).

| \( \delta \) | \( \tau = 2.01 \) | \( \tau = 4 \) |
|---|---|---|
| \( k_\ast \) | Error_{k_\ast} | Res_{k_\ast} | \( k_\ast \) | Error_{k_\ast} | Res_{k_\ast} |
| 0.1 | 58 | 135% | \( 2.0 \times 10^{-1} \) | 0 | 168% | \( 2.6 \times 10^{-1} \) |
| 0.1/5 | 167 | 50% | \( 4.0 \times 10^{-2} \) | 144 | 62% | \( 7.9 \times 10^{-2} \) |
| 0.1/5² | 203 | 42% | \( 7.8 \times 10^{-3} \) | 187 | 44% | \( 1.6 \times 10^{-2} \) |
| 0.1/5³ | 17421 | 39% | \( 1.6 \times 10^{-3} \) | 241 | 40% | \( 3.2 \times 10^{-3} \) |
| 0.1/5⁴ | 267460 | 24% | \( 3.2 \times 10^{-4} \) | 88535 | 34% | \( 6.4 \times 10^{-4} \) |
| 0.1/5⁵ | 1128345 | 4% | \( 6.4 \times 10^{-5} \) | 725625 | 10% | \( 1.3 \times 10^{-4} \) |

**Figure 2.** For Example 3.1 the plot on the left is for \( \delta = 0.02 \) and shows the conductances as functions of the spatial variable. The red line is the exact solution, and the green and blue light line are the approximations obtained for \( \tau = 2.01 \) and \( \tau = 4 \). The blue curve is the initial guess of our iterative procedure. The plot on the right is for \( \delta = 0.02 \) and displays the percentile error and the residual as functions of the iteration number. Furthermore, it shows the “stopping time” for both values of \( \tau \).

For the two experiments \( N_{ion} = 1, E_K = 2, L = 4, c = 1, T = 1, g(t, x) = g_K(t, x) \) and

\[
p(t) = p_F(t) = p_B(t) = \exp(t), \quad q(t) = q_F(t) = q_B(t) = \exp(t).
\]

The goal of this example is to find \( g_K(t, x) = (x - 2) \exp(-(x - 2)^2 - (4t - 2)^2) \) given \( V_F^\delta |_{\Gamma} = V_F^\delta (\cdot, \cdot) \) and \( V_B^\delta |_{\Gamma} = V_B^\delta (\cdot, \cdot) \).
Given \( g_K \), we compute \( V^\delta_E(\cdot, \cdot) \) according to (3) and (22), and we compute \( V^\delta_B(\cdot, \cdot) \) according to (18) and (22). We consider the initial guess \( g^{1,\delta}(t, x) = 0 \), and set both the time step and the mesh size as 1/64.

We present in Table 3 the results for various levels of noise.

| \( \delta \) | \( \tau = 4 \) | \( \tau = 6 \) |
|---|---|---|
| \( k_\ast \) | \( \text{Error}_{k_\ast} \) | \( \text{Res}_{k_\ast} \) | \( k_\ast \) | \( \text{Error}_{k_\ast} \) | \( \text{Res}_{k_\ast} \) |
| 0.05 | 2 | 81% | 8.1 \times 10^{-2} | 1 | 100% | 8.1 \times 10^{-2} |
| 0.05/5 | 8 | 50% | 3.6 \times 10^{-3} | 4 | 67% | 6.5 \times 10^{-3} |
| 0.05/5^2 | 30 | 18% | 1.3 \times 10^{-4} | 23 | 23% | 2.6 \times 10^{-4} |
| 0.05/5^3 | 84 | 5% | 5.9 \times 10^{-6} | 66 | 7.2% | 1.1 \times 10^{-5} |
| 0.05/5^4 | 186 | 2.6% | 2.0 \times 10^{-7} | 152 | 2.7% | 4.6 \times 10^{-7} |
| 0.05/5^5 | 575 | 2.2% | 8.2 \times 10^{-9} | 360 | 2.3% | 1.8 \times 10^{-8} |

Table 3. Results related to Example 3.2. See Table 2 for a description of the contents.

Example 3.3. In this example we consider two different ions, \( \text{Na} \) and \( K \), where \( E_K = 1 \), \( E_{Na} = 2 \), \( L = 2 \), \( c = 1 \), \( T = 1 \), \( g(x) = (g_K(x), g_{Na}(x)) \) and

\[
    r(x) = \cos(x + \pi/2), \quad p(t) = \exp(-t), \quad q(t) = 0.
\]

The goal is to find \( g(x) = (\sin(x), \cos(x)) \) given \( V^\delta|_\Gamma = V^\delta(\cdot, \cdot) \). We compute \( V^\delta(\cdot, \cdot) \) according to (3) and (22), and as initial guess we set \( g^{1,\delta}(x) = (3x, \exp(x)) \). The time step is 1/64 and the spatial mesh size is 1/128.
Figure 4. For the Example 3.2 and $\delta = 0.05/5^3$, the above figure displays the approximation error (red line) and the residual (green line). The algorithm stops at $k_* = 84$ for $\tau = 4$, and at $k_* = 66$ for $\tau = 6$.

In Table 4 we present the results for various levels of noise.

| $\delta$ | $\tau = 2.01$ | $\tau = 4$ |
|----------|---------------|-------------|
|          | $k_*$         | $\text{Error}_{k_*}$ | $\text{Res}_{k_*}$ | $k_*$         | $\text{Error}_{k_*}$ | $\text{Res}_{k_*}$ |
| $10^0$   | 1             | 645%        | $9.4 \times 10^{-1}$ | 1             | 645%        | $1.8 \times 10^{0}$   |
| $10^{-1}$| 39            | 310%        | $2.0 \times 10^{-1}$ | 27            | 373%        | $3.9 \times 10^{-1}$   |
| $10^{-2}$| 1366          | 70%         | $2.0 \times 10^{-2}$ | 601           | 142%        | $4.0 \times 10^{-2}$   |
| $10^{-3}$| 3182          | 25%         | $2.0 \times 10^{-3}$ | 2411          | 35%         | $4.0 \times 10^{-3}$   |
| $10^{-4}$| 17138         | 17%         | $2.0 \times 10^{-4}$ | 9021          | 19%         | $4.0 \times 10^{-4}$   |
| $10^{-5}$| 241044        | 8%          | $2.0 \times 10^{-5}$ | 100764        | 10%         | $4.0 \times 10^{-5}$   |

Table 4. Results for Example 3.3. See Table 2 for a description of the contents.

Example 3.4. As a particular case of (20), the set of edges is $\mathcal{E} = \{e_1, e_2, e_3\}$, the set of vertices $\mathcal{V} = \{\nu_1, \nu_2, \nu_3, \nu_4\}$, the border points $\partial \Theta = \{\gamma_1, \gamma_2, \gamma_3\}$, with one bifurcation point, as in Figure 1. The edge $e_1$ has vertices $\nu_1$ and $\nu_2$, the edge $e_2$ has vertices $\nu_2$ and $\nu_3$, finally the edge $e_3$ has vertices $\nu_2$ and $\nu_4$. The length of the edges are: $|e_1| = 1$, $|e_2| = 1$ $e$ $|e_3| = 2$. The numerical value of the vertices are: $\nu_1 = 0$, $\nu_2 = 1$, $\nu_3 = 2$ $e$ $\nu_4 = 3$. The numerical value of the border points are: $\gamma_1 = 0$, $\gamma_2 = 2$ $e$ $\gamma_3 = 3$. We denote by $V^i = V|_{e_i}$ the restriction of $V$ to the edge $e_i$. In this example $N_{\text{ion}} = 1$, $I_{\text{ion}} = \{K\}$, $E_K = 2$, $c = 2$, $T = 1$. 
Figure 5. For Example 3.2 with noise threshold $\delta = 4 \times 10^{-4}$ and $\tau = 6$. Figure 2-a and 2-b display the exact and approximate solutions (after $k_*$ iterations). Figure 2-c displays the absolute value of the approximation error.

For a point $p \in \Theta$ we define the initial condition,

$$V(0, p) = \begin{cases} 
\text{dist}(\nu_1, p) + 2 & \text{if } p \in e_1, \\
\text{dist}(\nu_2, p) + 3 & \text{if } p \in e_1 \cup e_2,
\end{cases}$$

where $\text{dist}(a, b)$ is the distance between the points $a$ and $b$, the function $V(0, \cdot)$ is continuous.

The boundary conditions are: $V_x(t, \gamma_1) = 2t$, $V_x(t, \gamma_2) = \cos(t)$ and $V_x(t, \gamma_3) = 0$. The condition at the bifurcation point is $V_{xx_3}(t, \nu_2) - V_{xx_2}(t, \nu_2) - V_{xx_3}(t, \nu_2) = 0$.

The goal of this example is to find $g_K(x) = \exp(x)$ given $V(\cdot, \cdot)$. Thus, given $g_K$, we compute $V^\delta(\cdot, \cdot)$ according to (20) and (22). We consider the initial guess $g^1, \delta(t, x) = \sin(x)$. The time step is $1/300$ and the spatial mesh size is $1/61$. In Table 7 we present the results for various levels of noise.

The $x$-axis of figure 8-a corresponds to the edge $e_1$, the $x$-axis of figure 8-b corresponds to the edge $e_2$ and the $x$-axis of figure 8-c corresponds to the edge $e_3$. 
Figure 6. Results for Example 3.3 with $\delta = 10^{-2}$. The left plot is related to $g_K = \sin(x)$, and the right plot is related to $g_{Na} = \cos(x)$. The red lines are the exact solutions, the blue line are the initial guesses and the green and blue lines are the final approximations for $\tau = 2.01$ and $\tau = 4$.

Figure 7. For Example 3.3 with $\delta = 0.1$ we plot the error (red line) and the residue (green line). For $\tau = 2.01$ the algorithm stops at $39 = \exp 3.6$, and for $\tau = 4$ it stops at $k^* = 27 = \exp 3.3$.

4. Conclusions

In this paper we develop and test a numerical scheme to find conductances of a passive cable. This has important applications and neuroscience, and is a hard problem. The method showed promising results, and the even harder problem of determining the conductances of “real” (i.e., nonlinear) neurons is currently under investigated.

The Landweber method (6) has a somewhat straightforward description, but is not practical in the original formulation. Indeed, computing the adjoint of the Gâteaux derivative seems
impossible in general. The development of auxiliary equations to overcome such hurdle is more art than science, and is done in a case-by-case basis.

However, when the method can be implemented, it yields good results even in the presence of noise, as shown here. It is also general enough to accommodate for different geometries (straight cables and trees), and different measured data (end point, whole cable).
Appendix A. Abstract Formulation

In practice, $V(\cdot, 0)$ and $V(\cdot, L)$ are part of the data. To account for the possibility of measurement noise we denote the actual measured data by $V^\delta(\cdot, 0)$ and $V^\delta(\cdot, L)$. Given $V^\delta$ and under the assumption that (3) holds, the inverse problem under consideration is to recover or approximate the conductances $g_i$.

The lack of stability characteristic of ill-posed problems can by tamed by regularization methods [16, 23, 26], in particular by the non-linear Landweber method, that we describe next.

Consider the Hilbert spaces $\mathcal{H}_1$ and $\mathcal{H}_2$, with inner-products $\langle \cdot, \cdot \rangle_{\mathcal{H}_i}$ for $i = 1, 2$, and the operator $F : \mathcal{D}(F) \to \mathcal{H}_2$, where $\mathcal{D}(F) \subset \mathcal{H}_1$ is the domain of $F$, not necessary a Hilbert space. Assume that $F(X) = Y$, and that $Y^\delta$ is known and represents a “noisy approximation” of the data $Y$, where for a given $\delta > 0$,

$$\|Y - Y^\delta\|_{\mathcal{H}_2} \leq \delta.$$ 

Our goal is to find an approximation for $X$.

The Landweber iteration defines $X^{k, \delta}$ by

$$X^{k+1, \delta} = X^{k, \delta} + F'(X^{k, \delta})^* (Y - F(X^{k, \delta})).$$

(24)

For each fixed $X^{k, \delta}$, the Gâteaux derivative $F'(X^{k, \delta}) : \mathcal{D}(F) \to \mathcal{H}_2$ defines a linear operator such that for each $\widetilde{X} \in \mathcal{D}(F)$,

$$F'(X^{k, \delta})(\widetilde{X}) = \lim_{t \to 0} \frac{F(X^{k, \delta} + t\widetilde{X}) - F(X^{k, \delta})}{t}.$$

Note in particular that it is possible to extend the domain of $F'(X^{k, \delta})$ to $\mathcal{H}_1$ when $F'(X^{k, \delta})$ is bounded and $\mathcal{D}(F)$ is dense in $\mathcal{H}_1$. We assume that.
The adjoint operator $F'(X^{k,\delta})^* : \mathcal{H}_2 \to \mathcal{H}_1$ is such that
\[
\langle F'(X^{k,\delta})^* \tilde{Y}, \tilde{X} \rangle_{\mathcal{H}_1} = \langle \tilde{Y}, F'(X^{k,\delta}) \tilde{X} \rangle_{\mathcal{H}_2} \quad \text{for all } \tilde{X} \in \mathcal{H}_1, \tilde{Y} \in \mathcal{H}_2.
\]

One possible stopping criteria for the iterative scheme (24) is given by the discrepancy principle, i.e., the iteration stops at the minimum $k^*_\delta = k(\delta, \mathcal{Y}^{\delta})$, such that, for a given $\tau > 2$,
\[
\| \mathcal{Y}^{\delta} - F(X^{k^*_\delta}) \|_{\mathcal{H}_2} \leq \tau \delta.
\]

It is possible to show that, under certain conditions, $X^{k^*_\delta}$ converges to a solution of $F(X) = \mathcal{Y}$ as $\delta \to 0$ [23] *Theorem 2.6.

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