Subthreshold Linear Modeling of Dendritic Trees: A Computational Approach

Alireza Khodaei[1] and Massimiliano Pierobon[1]

Abstract— **The design of communication systems based on the transmission of information through neurons is envisioned as a key technology for the pervasive interconnection of future wearable and implantable devices. While previous literature has mainly focused on modeling propagation of electrochemical spikes carrying natural information through the nervous system, in recent work the authors of this paper proposed the so-called subthreshold electrical stimulation as a viable technique to propagate artificial information through neurons. This technique promises to limit the interference with natural communication processes, and it can be successfully approximated with linear models. In this paper, a novel model is proposed to account for the subthreshold stimuli propagation from the dendritic tree to the soma of a neuron. A computational approach is detailed to obtain this model for a given realistic 3D dendritic tree with an arbitrary morphology. Numerical results from the model are obtained over a stimulation signal bandwidth of 1KHz, and compared with the results of a simulation through the NEURON software.**

I. Introduction

The study of neurons as means to propagate information between future wearable and implantable devices through the human body is encouraged by their ubiquitous distribution within the body and the existence of well-established techniques for their electrical interfacing [13], and novel emerging nanotechnology-enabled devices for their stimulation [1], [10]. Previous literature has mainly focused on the propagation of electrochemical spikes (action potentials) through neurons [3]. While this is an already extensively studied process that underlies the natural propagation of information through the nervous system, its exploitation for the design of communication systems presents problems mainly related to the interference with natural communications, and its non-linear nature.

In a previous contribution [7], we proposed a communication system based on the transmission of information through a neuron without active generation of action potentials, through the use of the so-called subthreshold electrical stimulation [12]. The propagation of subthreshold stimuli through neurons is usually reasonably approximated with linear models in neurophysiology literature [8]. This technique will have the advantage of limiting the interference with the aforementioned natural communications based on electrochemical spikes, since the subthreshold stimuli do not generally propagate from one neuron to another in the general case of chemical synapses [16]. Multiple neurons communication is also imaginable through neural circuits with electrical junctions (e.g. reflex paths). Our technique sets stage to realizing a sub-band communication paradigm in parallel with natural communication within neural system comparable with the way that ADSL technique exploits unused bandwidth of phone lines. However, neuron survivability concerns should be regarded as the extra injected electrical charge to the neuron changes the normal intracellular ion concentrations.

While in [7] we developed a model of the propagation of subthreshold stimuli from the neuron main body, *i.e.*, soma, to a remote location along the neuron's main length projection, *i.e.*, axon, in this paper we focus on modeling the propagation of these stimuli from the electrically-conductive projections that usually receive stimuli from other neurons, called dendrites, to the soma. While a model of the propagation of electrochemical spikes through dendrites, branched into dendritic trees, is presented in [4], in our work we focus on the very different subthreshold stimulation and the aforementioned linear approximations. In particular, in this paper we detail a computational model and its implementation to obtain the voltage at the soma resulting from a subthreshold current stimulation at the extremities of the dendrites for a given realistic 3D dendritic tree with an arbitrary morphology over a stimulation signal bandwidth of 1KHz. The numerical results from the proposed model show a good agreement with results computed from a realistic neuron simulation based on the non-linear and more general Hodgkin-Huxley model [12], performed in the NEURON [5] software.

The rest of the paper is organized as follows. In Sec. II we detail the main elements and assumptions of the proposed computational model, while in Sec. III we present the implementation of a computational tool based on this model. In Sec. IV we present numerical results to validate the proposed model against more realistic simulation environments. Finally, in Sec. V we conclude the paper.

II. Computational Model of a Dendritic Tree in Subthreshold Regime

In Fig. 1 we show a scheme of the computational model detailed in this section. In particular, we consider only the portion of a neuron within the **Nervous System** composed of the **Soma**, which is the main cell's body that contains the nucleus and other organelles, and the dendritic tree, which is

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[1]Alireza Khodaei and Massimiliano Pierobon are with the Department of Computer Science and Engineering, University of Nebraska-Lincoln, Lincoln, Nebraska 68588, USA {akhodaei,pierobon}@cse.unl.edu

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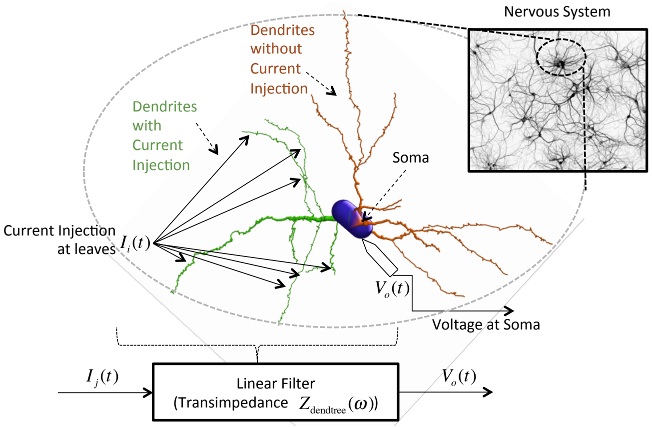

Fig. 1: Scheme of the proposed computational model of a dendritic tree. The neuron morphology shown in the figure has been generated through [2].

an arbitrary hierarchical branching of **Dendrites**, electrically-conductive projections from the soma [12]. Along the dendrites, special protrusions called dendritic spines allow the connection of the dendritic tree to multiple other neurons, which send electrochemical signals to the dendritic spines through their corresponding extremities, or synapses. Neurons are in general composed also of an axon, a thicker and longer projection from the soma that propagates the electrical excitation along its length and terminates into the synapses. The electrical properties of the dendritic tree, soma, and axon derive from the fact that the neuron is bound by a lipid bylayered membrane that maintains a difference between inner and outer concentrations of ions (electrically-charged molecules), resulting in an electrical potential across the membrane itself. We assume that when no external perturbation is applied to the neuron, the membrane potential is constant and homogeneous throughout the neuron, and equal to the resting potential E_m, in agreement with widely accepted models from the neurophysiology literature [15]. Nevertheless, in this paper we focus on the propagation of information between the extremities of the dendrites, also called leaves in the rest of the paper, and the soma. In particular, we abstract the transmission of information through the injection of electrical currents where a microelectrode penetrates the membrane at each leaf and releases electrical current into the intracellular space [13]. The injected current, and the consequent local perturbation of the membrane potential around its resting potential, are propagated through the dendritic tree until reaching the soma. We assume that the reception is realized through an intracellular electrode through which we read the membrane voltage $V_o(t)$ at the soma.

In our previous publication [7], we modeled the propagation of information as a linear communication channel between the soma and a remote location of the axon in similar conditions (subthreshold regime), where we considered the complete dendritic tree as an impedance load connected to the soma, with no input to any dendrite. In this paper, we detail the computational model and the development of a tool to model the propagation of information from a subset

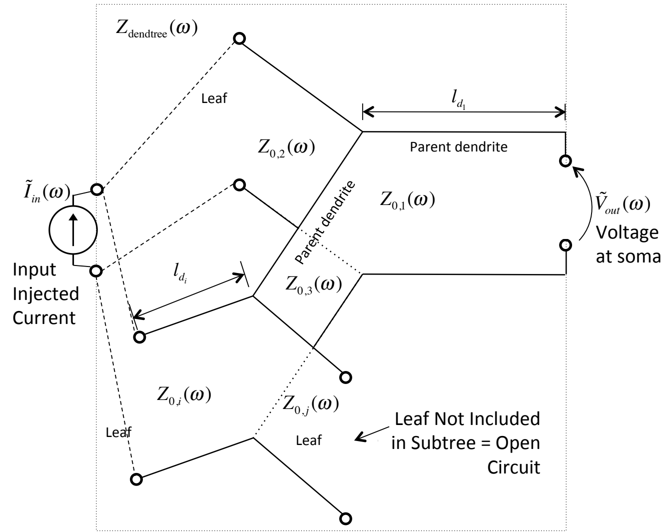

Fig. 2: Transmission line model of the dendritic tree used for the computation of the transimpedance $Z_{\mathrm{dendtree}}(\omega)$.

of leaves of the dendritic tree, *i.e.*, those abstracting the connection from a single presynaptic neuron, to the soma. As shown in Fig. 1, we propose a system model where the input is a modulated current $I_{in}(t)$ as function of the time t injected at the aforementioned leaves, and the output is the resulting membrane voltage $V_o(t)$ at the soma. The proposed model is expressed as a linear filter in the frequency ω domain as follows:

$$\tilde{V}_{out}(\omega) = Z_{\mathrm{dendtree}}(\omega)\tilde{I}_{in}(\omega)\,, \tag{1}$$

where $\tilde{I}_{in}(\omega)$ and $\tilde{V}_{out}(\omega)$ are the Fourier transforms of $I_{in}(t)$ and $V_{out}(t)$, respectively, and $Z_{\mathrm{dendtree}}(\omega)$ is the transimpedance of the dendritic subtree, defined here as the portion of the dendritic tree that is connected to a single presynaptic neuron, and it is computed through (1).

A. The Subthreshold Condition

The linear filter model expressed in (1) is valid only when the membrane potential maintains a value less than V_{th} at the soma, named subthreshold condition [12]. This is realized when the current $\tilde{I}_{in}(\omega)$ injected into the dendritic tree satisfies the subthreshold stimulation condition, expressed as

$$\tilde{I}_{in}(\omega) : \tilde{V}_{out}(\omega) < V_{th}\,, \tag{2}$$

V_{th} typically ranges from -60mV to -55mV, depending on the electrophysiological characteristics of the neuron [12]. Whenever the subthreshold condition is satisfied, the dendritic tree can be modeled as a branched transmission line through Cable Theory [14], as shown in Fig 2 and detailed in the following.

B. The Dendritic Tree Transimpedance $Z_{\mathrm{dendtree}}(\omega)$

The dendritic tree transimpedance $Z_{\mathrm{dendtree}}(\omega)$, defined in (1) as the ratio between the voltage $\tilde{V}_{out}(\omega)$ at the soma and the current $\tilde{I}_{in}(\omega)$ injected at the leaves connected to a single presynaptic neuron, is computed through a branched transmission line model, shown in Fig. 2. In this model, each dendrite i is modeled by a transmission line with characteristic impedance $Z_{0,i}(\omega) = \sqrt{4R_a Z_m(\omega)/(\pi^2 d_i^3)}$, d_i being the dendrite's diameter, and length equal to the physical length of the dendrite l_{d_i}.

To analytically compute $Z_{\text{dendtree}}(\omega)$, we make the following assumptions:

- The current injected at the leaves $\tilde{I}_{in}(\omega)$ and resulting in a voltage $\tilde{V}_{out}(\omega)$ at the soma is equal to the current that would result at the soma $\tilde{I}_{soma}(\omega)$ by applying a voltage $\tilde{V}_{out}(\omega)$ in the condition where the same leaves have zero impedance at their terminals (short circuit).
- The leaves that do not receive current injection in our model are considered as open circuits.

These assumptions are justified by taking into account the linearity and reciprocity of the transmission line abstraction of the dendritic tree, which can be considered as a two-port electrical network where one port corresponds to the terminals of the soma, and the other port corresponds to the terminals connected to the injected current $\tilde{I}_{in}(\omega)$, in parallel to the terminals of the dendrite subtree leaves, as shown in Fig. 2.

As a consequence, we can have the following equivalence:

$$Z_{\text{dendtree}}(\omega) = Z_{\text{soma}}(\omega)\,, \tag{3}$$

where $Z_{\text{soma}}(\omega)$ is the impedance that would be observed at the soma when the dendritic subtree leaves have their terminals in short circuit, and the remaining leaves are open circuits. This can be computed through the computational procedure that we proposed in [7], which is a recursive algorithm based on a post-order traverse method [6], as detailed in Algorithm 1.

Algorithm 1 Recursive Calculation of $Z_{soma}(\omega)$

procedure DendTreeSomaImpedance ($node$ dendrite)
  if dendrite ! = NULL **then**
    for $node$ i : dendrite.GetChildren () **do**
      DendTreeSomaImpedance (i)
      Compute $Z_{soma}(\omega) = Z_{d,i}(\omega)$ with (4)

The impedance $Z_{d,i}(\omega)$ at a dendrite i is obtained in [7] by applying Transmission Line Theory [11] to the transmission line abstraction shown in Fig. 2. This is expressed as follows:

$$Z_{d,i}(\omega) = Z_{0,i}(\omega) \cdot \frac{Z_{L,i}(\omega)\cosh(\gamma(\omega) l_{d_i}) + Z_{0,i}(\omega)\sinh(\gamma(\omega) l_{d_i})}{Z_{L,i}(\omega)\sinh(\gamma(\omega) l_{d_i}) + Z_{0,i}(\omega)\cosh(\gamma(\omega) l_{d_i})}\,, \tag{4}$$

where $\gamma(\omega) = \sqrt{4R_a/\Re[Z_m(\omega)] d_i}$, R_a is the axial resistance, a parameter determined experimentally, and $Z_m(\omega)$ is the transmembrane impedance, detailed in [7]. If dendrite i is a leaf subject to current injection, the load $Z_{L,i}(\omega) = 0$, otherwise, if the dendrite i is a leaf without current injection, $Z_{L,i}(\omega) \to \infty$. Finally, if the dendrite i is a parent, $Z_{L,i}(\omega)$ is expressed as the equivalent load of N parallel transmission lines branching from the dendrite i. This is expressed as follows:

$$Z_{L,i}(\omega) = \frac{\sum_{n=1}^{N} Z_{d,n}(\omega)}{\prod_{n=1}^{N} Z_{d,n}(\omega)}\,, \tag{5}$$

where N is the number of dendrites branching out from dendrite i, and $Z_{d,n}(\omega)$ is the impedance of the dendrite n computed at an earlier step in the recursion of Algorithm 1.

It is also possible to demonstrate that the computational procedure in Algorithm 1 can be simplified by not accounting for dendritic tree branches connected to leaves that do not receive current injection. In fact, by substituting the open circuit load in the expression in (5), the the time on which impedance $Z_{st,i}(\omega)$ of a leaf dendrite i without current injection can be expressed as

$$Z_{st,i}(\omega) = -\mathrm{j} Z_{0,i}(\omega)\cot(\beta l_i)\,, \tag{6}$$

where $\beta = 2\pi/\lambda$, λ is the signal wave length, l_i is the length of the leaf dendrite i, and cot the cotangent function. Given that the length of a dendrite is in the order of micrometers [12], and the frequency range that we consider in our model is in the order of kHz, the resulting $Z_{st,i}(\omega)$ will likely assume much higher values than parallel branches connected to short circuit loads at the leaves subject to the current injection, and can be safely removed from the computation in Algorithm 1.

III. Computational Tool Implementation

Algorithm 2 Implementation of $Z_{Soma}Calculation$

procedure LeavesImpedance ($list$ DendriticTree)
  $list$ LeavesList = Leaf dendrites of DendriticTree
  $list$ Compute $Z_{LeafDendrite_i}$ with (4) by having $Z_L \to 0$
procedure ParentsImpedance ($list$ LeavesList)
  $list$ ParentList = All parents if LeavesList nodes
  for $node$ Parent_i in ParentList **do**
    if Parent_i already computed **then**
      Break
    else
      $list$ ChildList = Children of Parent_i
      for $node$ Child_j in ChildList **do**
        if Child_j has any child **then**
          $list$ GrandChildrenList = Children of Child_j
          RecursiveCount ++
          ParentsImpedance(GrandChildrenList)
          RecursiveCount - -
          $Z_{L,Parent_i}$ = Parallel lump all Child_j
        else $Z_{L,Parent_i}$ = Parallel lump all Child_j
    Compute $Z_{ParentDendrite_i}$ with (4)
  if RecursiveCount == 0 **then**
    ParentsImpdance(ParentList)

Algorithm 2 lists the steps we took in our implementation. First of all, we separate out the leaves of the given dendritic tree and set their load impedance to zero. When a parent dendrite is visited, the software identifies all possible children subtrees, calculates their impedances, and lumps them considering they are in parallel. This implementation is compatible with the fact that the impedance of a parent

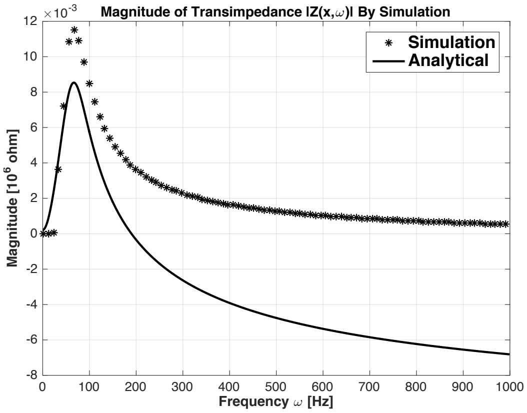

Fig. 3: Magnitude of the dendritic tree transimpedance $Z_{\mathrm{dendtree}}(\omega)$ for frequencies ω ranging from 1 Hz to 1000 Hz

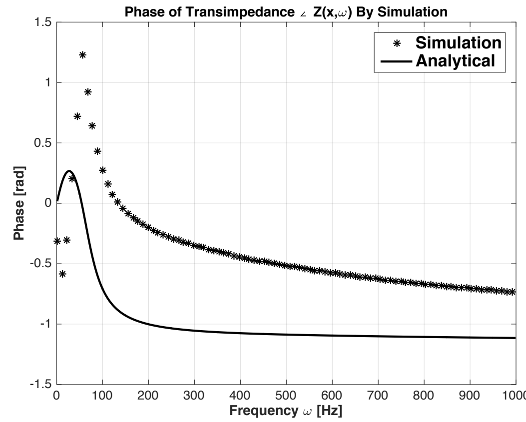

Fig. 4: Phase of the dendritic tree transimpedance $Z_{\mathrm{dendtree}}(\omega)$ for frequencies ω ranging from 1 Hz to 1000 Hz

neurite depends on the parallel-lumped impedance of all the children's impedances that are connected to its leaky end, as expressed in (4) [7]. In the case that the impedance of a child subtree is not yet computed, we have to recursively call (4) for this subtree.

IV. Numerical Results

We present a preliminary comparison of numerical results obtained by running the proposed computational model in Sec. II through the computational tool detailed in Sec. III, with results of simulations performed through the NEURON software [5]. We based our results on the biophysical parameters of the giant squid axon, which are considered as standard for neurophysiology model comparison [9]. These parameters are detailed in our previous publication [7]. The dendritic tree morphology corresponds to the pyramidal neuron in the nerocortex of the human brain named 2a pyramidal2aF, and it is extracted from the NeuroMorpho database [2]. The 2a pyramidal2aF was chosen since it does not have axon, and pyramidal neurons are well investigated in neurology.

Fig. 3 and Fig. 4 show the magnitude and the phase, respectively, of the dendritic tree transimpedance $Z_{\mathrm{dendtree}}(\omega)$. It is important to observe that we have a maximum (resonant frequency) at 67 Hz, and the general trend of both magnitude and phase are in agreement in both the computational tool and NEURON simulation results.

V. Conclusion

In this paper, a novel model is proposed to account for the subthreshold stimuli propagation from the dendritic tree to the soma of a neuron. In particular, in this paper we detail a computational model and its implementation to obtain the voltage at the soma resulting from a subthreshold current stimulation at the extremities of the dendrites. Our model takes into account any given realistic 3D dendritic tree with an arbitrary morphology. Numerical results from the model are obtained over a stimulation signal bandwidth of 1KHz, and compared with the results of a simulation through the NEURON software. We believe that this model will contribute to the understanding of the propagation of information in neuron in general, and in particular will go in the direction of enabling the future design of communication systems based on the transmission of information between neuronal-interfaced devices, such as those envisioned within the paradigm of the Internet of Bio-Nano Things [1].

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