On General Nonlinearities in Ephaptic Coupling

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November 25, 2023

Abstract

In this paper, the authors present the Crank Nicolson formulae for simulation of nonlinearities introduced in the current-coupling term of the coupled-axon governing equation of Reutskiy *et al.* (2003). The exact matrix equation is obtained for this case. The setting is also generalized to higher order nonlinearities.

1 Introduction

Nonlinear phenomena are widespread in nature Scott (2007). Furthermore, many electronic devices have nonlinear current-voltage characteristics. The nervous system is often modeled using an analogy with electronic circuits. It is but natural therefore to consider that there might be nonlinear aspects to its behavior.

In (Kitahata *et al.*, 2009) the authors look at coupling and synchronization of candle flames. They find the presence of nonlinear coupling terms of the form σT^n where σ is the Stefan-Boltzmann constant and T is the temperature of the flame under consideration. n ranges from 2 to 4 and in all cases allowed for synchronization between flames. Motivated and intrigued by the possibility of similar terms in the ephaptic case (see Equation (7) in (Reutskiy *et al.*, 2003)), and what their impact might be, the authors investigate their presence herein. Whereas the nonlinearity is well-justified by Kitahata et. al., in our case the motivation comes from earlier (unpublished) attempts to model action potential propagation in a single axon using the nonlinear Burgers'-Huxley equation (Yefimova & Kudryashov, 2004).

This paper studies the discretization of the nonlinear equations obtained by considering a very basic nonlinear coupling where the coupling transmembrane voltage pre-multiplies the second partial derivative with respect to position. Related references include Boldrighini *et al.* (2012), Li & Sinai (2010) and Li & Sinai (2008).

The paper is organized as follows: In Section 2 we present the notation to be used in this paper as well as a recap of three principal axon models prevalent in the literature. In Section 3, we present the multiple-axon ephaptic equation in its standard form. In Section 4 we introduce the nonlinearity and in Section

5 we discretize it. In Section 6 we generalize the nonlinearity and discretize it. Finally, in Section 7 we conclude with a discussion.

2 Preliminaries

The precursors to the nonlinear equation of this paper are: the Hodgkin-Huxley equation Hodgkin & Huxley (1952b,a), the Reutskiy equation Reutskiy *et al.* (2003) and the geometrical ephaptic equation Chawla *et al.* (2019). We present here a table which contains the notation used in this paper.

S.No.	Symbol	Meaning
1	C_i	capacitance of the i-th axon's myelin sheath, per unit length Chawla *et al.* (2019)
2	V_i	transmembrane voltage of the i-th axon
3	(x,t)	(space,time)-variables
4	$\kappa, \varsigma_k, \xi, \alpha, \beta$	constants
5	G	conductance per unit length
6	$I^{ion,inj}$	(ionic,injected) current
7	L	number of spatial discretizations
8	$\overrightarrow{x}^{n+1}$	systematized vector of transmembrane voltages at the $(n+1)$-th time instant
9	F	order of the general nonlinearity

Table 1: Symbols and their meanings as used in this manuscript.

3 The Coupled Equation

The multiple-axon equation is,

$$C_i \frac{\partial V_i}{\partial t} = \kappa \frac{\partial^2 V_i}{\partial x^2} + \sum_{k \neq i} \varsigma_k \frac{\partial^2 V_k}{\partial x^2} - \xi G V + (1-\xi) I^{ion,inj} \tag{1}$$

and we wish to modify the coupling term. Note that whether we introduce a voltage-squared in place of a voltage in the coupling sum or in the term outside and prior to the coupling sum, we will have to deal with discretization of terms of the form,

$$V_i \frac{\partial^2 V_i}{\partial x^2}. \tag{2}$$

This is the nature of the basic nonlinearity. For basic details on discretization, we refer the reader to Crank and Nicolson's original paper (Crank & Nicolson, 1947).

4 Introduction of Nonlinearity

We begin with the two equations which are to be discretized after nonlinearization,

$$C_1 \frac{\partial V_1}{\partial t} = \kappa_1 \frac{\partial^2 V_1}{\partial x^2} + \varsigma_2 \frac{\partial^2 V_2}{\partial x^2} - G_1 V_1 \tag{3}$$

and

$$C_2 \frac{\partial V_2}{\partial t} = \kappa_2 \frac{\partial^2 V_2}{\partial x^2} + \varsigma_1 \frac{\partial^2 V_1}{\partial x^2} - G_2 V_2. \tag{4}$$

While several types of nonlinearities might be considered, we will discretize the following two coupled nonlinear equations:

$$C_1 \frac{\partial V_1}{\partial t} = \kappa_1 \frac{\partial^2 V_1}{\partial x^2} + \varsigma_2 V_2 \frac{\partial^2 V_2}{\partial x^2} - G_1 V_1 \tag{5}$$

and

$$C_2 \frac{\partial V_2}{\partial t} = \kappa_2 \frac{\partial^2 V_2}{\partial x^2} + \varsigma_1 V_1 \frac{\partial^2 V_1}{\partial x^2} - G_2 V_2. \tag{6}$$

The nonlinear term can be discretized by viewing it as the product of two terms whose individual discretizations are known. The remaining terms are quite standard and commonplace.

5 Crank-Nicolson Discretization of Nonlinearity

We start with Equation (5)

$$C_1 \frac{\partial V_1}{\partial t} = \kappa_1 \frac{\partial^2 V_1}{\partial x^2} + \zeta_2 V_2 \frac{\partial^2 V_2}{\partial x^2} - G_1 V_1. \tag{7}$$

We will use the following discretization formulae to discretize the overall equation: $\frac{\partial V_1}{\partial t}$ can be discretized as

$$\frac{V_1(i, n+1) - V_1(i, n-1)}{2\triangle t}, \tag{8}$$

$\frac{\partial^2 V_1}{\partial x^2}$ can be discretized as

$$\frac{V_1(i+1, n) - 2V_1(i, n) + V_1(i-1, n)}{(\triangle x)^2}, \tag{9}$$

V_2 as

$$\frac{1}{2}[V_2(i, n+1) + V_2(i, n-1)] \tag{10}$$

and $\frac{\partial^2 V_2}{\partial x^2}$ as

$$\frac{V_2(i+1,n) - 2V_2(i,n) + V_2(i-1,n)}{(\triangle x)^2}. \tag{11}$$

Assuming 'zero' initial conditions, at time $n = 1$ we have:

$$\alpha_1 V_{1,i}^2 = \beta_2 V_{2,i}^2 [V_{2,i+1}^1 - 2V_{2,i}^1 + V_{2,i-1}^1] + \beta_1 [V_{1,i+1}^1 - 2V_{1,i}^1 + V_{1,i-1}^1] \tag{12}$$

and

$$\alpha_2 V_{2,i}^2 = \beta_1 V_{1,i}^2 [V_{1,i+1}^1 - 2V_{1,i}^1 + V_{1,i-1}^1] + \beta_2 [V_{2,i+1}^1 - 2V_{2,i}^1 + V_{2,i-1}^1]. \tag{13}$$

Next, we introduce the definition of R_1 as

$$V_{2,i+1}^1 - 2V_{2,i}^1 + V_{2,i-1}^1 \tag{14}$$

and S_1 as

$$V_{1,i+1}^1 - 2V_{1,i}^1 + V_{1,i-1}^1. \tag{15}$$

This leads to the following simplified system:

$$\alpha_1 V_{1,i}^2 = \beta_2 V_{2,i}^2 R_1 + \beta_1 S_1 \tag{16}$$

and

$$\alpha_2 V_{2,i}^2 = \beta_1 V_{1,i}^2 S_1 + \beta_2 R_1. \tag{17}$$

For a general time n, the system is:

$$\alpha_1 V_{1,i}^{n+1} = \beta_2 V_{2,i}^{n+1} R_n + \alpha_1 V_{1,i}^{n-1} + \beta_1 S_n - \beta_2 V_{2,i}^{n-1} R_n \tag{18}$$

and

$$\alpha_2 V_{2,i}^{n+1} = \beta_1 V_{1,i}^{n+1} S_n + \alpha_2 V_{2,i}^{n-1} + \beta_2 R_n - \beta_1 V_{1,i}^{n-1} S_n. \tag{19}$$

Next, we focus on the matrix equation corresponding to Equation (18). We have

$$\alpha_1 V_{1,i}^{n+1} - \beta_2 V_{2,i}^{n+1} R_n = \alpha_1 V_{1,i}^{n-1} + \beta_1 S_n - \beta_2 V_{2,i}^{n-1} R_n. \tag{20}$$

The various vectors involved in the above equation are as follows when the spatial index is explicit:

$$V_{1,i}^{n+1} = \begin{bmatrix} V_1(0,n+1) \\ V_1(1,n+1) \\ V_1(2,n+1) \\ V_1(3,n+1) \\ V_1(4,n+1) \\ . \\ . \\ . \end{bmatrix}, \tag{21}$$

$$V_{2,i}^{n+1} = \begin{bmatrix} V_2(0,n+1) \\ V_2(1,n+1) \\ V_2(2,n+1) \\ V_2(3,n+1) \\ V_2(4,n+1) \\ . \\ . \\ . \end{bmatrix}, \tag{22}$$

$$V_{1,i}^{n-1} = \begin{bmatrix} V_1(0,n-1) \\ V_1(1,n-1) \\ V_1(2,n-1) \\ . \\ . \\ . \\ . \\ . \end{bmatrix} \tag{23}$$

and

$$V_{2,i}^{n-1} = \begin{bmatrix} V_2(0,n-1) \\ V_2(1,n-1) \\ V_2(2,n-1) \\ . \\ . \\ . \\ . \\ . \end{bmatrix}. \tag{24}$$

Next we note that in matrix form the second term on the LHS of Equation (20) can be expressed as,

$$\beta_2 \cdot diag[V_2(0,n+1), V_2(1,n+1), V_2(2,n+1), ...]_{L+1\times L+1} \cdot R^n_{L+1\times 1}. \tag{25}$$

Thus, the nonlinearity stands resolved for computational purposes. Likewise, the last term on the RHS of Equation (20) can also be written out.

The algorithm to be followed is straightforward. We treat R_n as a constant and plug it on the LHS along with other n-type plugins on the RHS. We thus obtain the $n+1$-type terms. Then this process is repeated for every n. We require the simple representation of the following type of terms:

$$\alpha_1 \begin{bmatrix} V_{1,i}^{n+1} \\ . \\ . \\ . \\ . \end{bmatrix} - \beta_2 \cdot diag(V_{2,i}^{n+1}) R^n. \tag{26}$$

These can be written as:

$$\begin{bmatrix} \alpha_1 I, & -\beta_2 R^n \end{bmatrix} \begin{bmatrix} V_{1,i}^{n+1} \\ . \\ . \\ , \\ V_{2,i}^{n+1} \\ . \\ . \\ , \\ . \\ . \\ . \\ . \end{bmatrix} = RHS \tag{27}$$

which can succinctly be written as:

$$A_n \overrightarrow{x}^{n+1} = RHS^{\leq n} \tag{28}$$

and, upon inverting we can isolate the variable of interest:

$$\overrightarrow{x}^{n+1} = A_n^{-1} RHS^{\leq n} \tag{29}$$

Next, we look at the joint evolution of coupled equations. For the second axon, we can write similarly:

$$B_n \overrightarrow{x}^{n+1} = RHS_2^{\leq n} \tag{30}$$

where

$$B_n = \begin{bmatrix} -\beta_1 S^n, & \alpha_2 I \end{bmatrix} \tag{31}$$

and we make it a point to subscript the term RHS in Equation (28) with the subscript 1. Then we can put together equations (28) and (30) in a single matrix equation which can be propagated in time after inversion:

$$\boxed{\begin{bmatrix} A_n \\ B_n \end{bmatrix} \overrightarrow{x}^{n+1} = \begin{bmatrix} RHS_1^{\leq n} \\ RHS_2^{\leq n} \end{bmatrix} \qquad (32)}$$

In Equation (32), the superscript $\leq n$ indicates that the time instant of relevance is earlier than or equal to n.

6 General Nonlinearity and Its Discretization

Recall that we started the last section, Section 5, by using:

$$C_1 \frac{\partial V_1}{\partial t} = \kappa_1 \frac{\partial^2 V_1}{\partial x^2} + \zeta_2 V_2 \frac{\partial^2 V_2}{\partial x^2} - G_1 V_1. \tag{33}$$

This can be modified as follows, by introducing a quadratic pre-multiplier in the nonlinear term, instead ofthe linear pre-multiplicative factor:

$$C_1 \frac{\partial V_1}{\partial t} = \kappa_1 \frac{\partial^2 V_1}{\partial x^2} + \zeta_2 V_2^2 \frac{\partial^2 V_2}{\partial x^2} - G_1 V_1. \tag{34}$$

In general,

$$C_1 \frac{\partial V_1}{\partial t} = \kappa_1 \frac{\partial^2 V_1}{\partial x^2} + \zeta_2 V_2^F \frac{\partial^2 V_2}{\partial x^2} - G_1 V_1. \tag{35}$$

To discretize the F-th order general nonlinearity of Equation (35) using the Crank Nicolson method, we use the binomial expansion after replacing V_2 by its discretized version.

7 Discussion

In this paper, we studied the Crank-Nicolson discretization of Reutskiy's ephaptic coupling equations when a nonlinearity was introduced in them. The nonlinearity was further generalized and discretized. In future work, these discretized equations will be simulated extensively. All of the developments related to the $F = 0$ case can be replicated for general F.[1] For example, we can study focal demyelination, noisy ion channels, tortuous tracts and the machine learning analogy Chawla & Morgera (2022b). We can also study the impact of the general nonlinearity on universal quantum computation in the brain Chawla (2022); Chawla & Morgera (2022a). Furthermore the role of electric fields can also be explored in the nonlinear setting Chawla *et al.* (2021).

Nonlinear waves have long been considered in the axonal context, though there are almost no studies in the ephaptic setting. For example, solitons have been studied extensively Mattsson & Werpers (2016); Priya & Kavitha (2022); Scott *et al.* (1973); Cano & Dilão (2022). Unlike Mattsson & Werpers (2016) we did not consider methods other than the Crank-Nicoslon discretization method. The solitons considered in these papers are related to non-electrical aspects of nerve signaling. As such, it would be interesting to combine the study of non-electrical and electrical effects by juxtaposition. This would require additional theoretical work and can be taken up in future. There are also additional papers which have looked at other types of nonlinearities in neural networks and neurons Nfor *et al.* (2022); Zhou *et al.* (2023); Kakmeni *et al.* (2014); Achu *et al.* (2018).

[1] One can also link F itself to the geometry and inter-axonal distances by some form of proportionality. This could be useful in settings where the nonlinearity is due in part to the inter-axonal medium. Further, if the medium is noisy, F can be augmented with a random variable. This would then change the problem to one of the simulation of *stochastic* nonlinear partial differential equations. Considerations of information theory such as channel capacity and reliability can also be invoked in such a setting, as the multiple axons will act as sources and destinations for one another, forming a network.

In the context of these referenced efforts, the present work opens up the additional possibility that novel and interesting nonlinear effects in action potential propagation may arise in the current-coupled axonal setting.

Acknowledgment

AC thanks Prof. Salvatore Domenic Morgera of the University of South Florida for suggesting the study of nonlinear equations in the coupled-axon context.

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