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High-order accurate difference schemes for the Hodgkin–Huxley equations

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ABSTRACT

A novel approach for simulating potential propagation in neuronal branches with high accuracy is developed. The method relies on high-order accurate difference schemes using the Summation-By-Parts operators with weak boundary and interface conditions applied to the Hodgkin–Huxley equations. This work is the first demonstrating high accuracy for that equation. Several boundary conditions are considered including the non-standard one accounting for the soma presence, which is characterized by its own partial differential equation. Well-posedness for the continuous problem as well as stability of the discrete approximation is proved for all the boundary conditions. Gains in terms of CPU times are observed when high-order operators are used, demonstrating the advantage of the high-order schemes for simulating potential propagation in large neuronal trees.

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1. Introduction

Understanding the integration of synaptic input by a neuron and the propagation of the signal to its own output synapses is of high importance in neurosciences. Numerical simulation of such a phenomena has become an option since Hodgkin and Huxley developed their model in 1952 [1]. The Hodgkin–Huxley equations are a set of coupled partial and ordinary differential equations. The first one is the cable equation that describes the distribution and evolution of the intracellular potential. The other equations are related to the evolution of gating variables describing ion channels dynamics inside a neuron, which is typically constituted of dendritic branches, a soma, an axon and synapses. Appropriate boundary conditions can be associated with branch ends, junctions and the soma. The soma boundary condition is non-standard since it consists of a linear relation between time and space derivatives of the solution and the solution itself.

Subsequently, Rall developed methods for solving the potential propagation in passive neuronal trees where branches satisfying the “3/2” law are connected to the soma [2]. In the subsequent literature, the Hodgkin–Huxley equations were typically approximated using multi-compartmental models where each unknown corresponds to the value of the potential or gating variable inside a small compartment. Current conservation is then enforced, resulting in spatially second-order schemes such as in [3] where Hines simulated the potential propagation in a neuronal tree without soma. That scheme was subsequently used for predictions of potential propagation in dendritic trees with soma [4,5].

A method for time integration of the coupled system formed by the cable and gating variables equations was proposed by Hines in [3] using a second-order accurate staggered Crank–Nicolson method. A first-order in time backward Euler monolithic scheme for the coupled Hodgkin–Huxley equations of a single branch with Neumann boundary conditions was

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then proposed in [6] together with a convergence proof. In [7], the authors propose a first-order in time forward Euler scheme for the Hodgkin–Huxley equations with Dirichlet boundary conditions, as well as a convergence proof under a CFL condition.

In the present work, high-order accurate difference schemes based on Summation-By-Parts (SBP) operators with the weak Simultaneous Approximation Term (SAT) procedure [8–18] are applied to the Hodgkin–Huxley equations and their associated boundary conditions. Rigorous convergence properties are demonstrated for several types of boundary conditions, including the non-standard soma boundary condition. The ability to apply high-order schemes for the solution of the Hodgkin–Huxley equations is essential since it results in a lower computational cost for the large systems that arise when neurons with large dendritic trees are considered. It will be demonstrated that the SBP-SAT technique provides a modular approach that is particularly effective for coupling of branches in a dendritic tree. Indeed, the SBP-SAT method offers a very effective way to enforce potential continuity and current conservation at the junction between those branches.

This paper is organized as follows: in Section 2, the continuous set of partial differential equations and associated boundary conditions are presented and their strong well-posedness is demonstrated using energy estimates for two essential cases: (1) the case of an axon connected to the soma and (2) the case of a dendritic tree. In Section 3, discretization of each of the aforementioned problems is carried out and the associated penalty coefficients are chosen so that semi-discrete energy estimates hold. This results in identical estimates as in the continuous case and strong stability of the semi-discrete problem. In Section 4, the order of convergence associated with each of the two aforementioned problems is investigated using the method of manufactured solutions. Applications of the new proposed approach to large neuronal systems are reported in Section 5. Conclusions are drawn in Section 6.

2. The continuous problem

2.1. Equations

The Hodgkin–Huxley equations [1] are a set of coupled partial and ordinary differential equations expressed in terms of the (1) intracellular potential $u(x, t)$ and (2) gating variables $m(x, t)$, $h(x, t)$ and $n(x, t)$ describing ion channels dynamics. The computational domain is in this section $x \in [0, L]$.

The equation for the potential u is based on the cable equation [19] and can be written as

$$u_t = \frac{\mu}{a(x)} (a(x)^2 u_x)_x - \frac{1}{C_m} g(m(x, t), h(x, t), n(x, t)) u + \frac{1}{C_m} f(m(x, t), h(x, t), n(x, t), x, t), \quad (x, t) \in [0, L] \times [0, T]. \quad (1)$$

In (1), $a(x)$ is the radius of the neuron at the location x , C_m the specific membrane capacitance and

$$\mu = \frac{1}{2C_m R_i} > 0,$$

where R_i denotes the axial resistivity. The conductance $g(m, h, n)$ of the cable in terms of the gating variables is

$$g(m, h, n) = g_1 m^3 h + g_2 n^4 + g_3, \quad (2)$$

where $g_i > 0$, $i = 1, 2, 3$. The expression for $f(m, h, n, x, t)$ is given by

$$f(m, h, n, x, t) = g_1 E_1 m^3 h + g_2 E_2 n^4 + g_3 E_3 - I(x, t), \quad (3)$$

where E_i , $i = 1, 2, 3$ are equilibrium potentials. $I(x, t)$ is an input current at location x that originates either from artificial current injection or synaptic input from another neuronal cell.

The equations describing the evolution of the gating variables are

$$\begin{aligned} m_t(x, t) &= \alpha_m(u(x, t))(1 - m(x, t)) - \beta_m(u(x, t))m(x, t), \\ h_t(x, t) &= \alpha_h(u(x, t))(1 - h(x, t)) - \beta_h(u(x, t))h(x, t), \\ n_t(x, t) &= \alpha_n(u(x, t))(1 - n(x, t)) - \beta_n(u(x, t))n(x, t), \end{aligned} \quad (4)$$

where $(x, t) \in [0, L] \times [0, T]$. Expressions for α_m , α_h , α_n , β_m , β_h and β_n are provided in Appendix A.

One can prove the following property based on the equations associated with the gating variables.

Proposition 1. *Let $x \in [0, L]$. If $0 \leq m(x, 0) \leq 1$ and if $m(x, t)$ is C^0 in time, then $0 \leq m(x, t) \leq 1 \forall t \in [0, T]$.*

Proof. See Appendix B. \square

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