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Reduced model and simulation of myelinated axon using eigenfunction expansion and singular perturbation

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Abstract

In a myelinated axon, there exist many nodes of Ranvier where myelin sheaths are absent and action potentials are actively regenerated. Hence, a myelinated axon is a nonuniform cable where myelinated parts and unmyelinated nodes of Ranvier are described by different cable equations. For the modelling of a myelinated axon, the compartment model based on finite volume or finite difference discretization was dominantly used. In this paper, we propose a hybrid approach where an eigenfunction expansion combined with singular perturbation is employed for myelinated parts, and demonstrate that the proposed scheme can achieve an order of magnitude accuracy improvement for low order models. Moreover, it is also shown that the proposed scheme converges faster to attain a given accuracy. Hence, for simulation of myelinated axons, the proposed scheme can be an attractive alternative to the compartment model, that leads to a low order model with much higher accuracy or that converges faster for a given accuracy.

Keywords: Myelinated axon; Reduced model; Simulation; Eigenfunction expansion; Singular perturbation

1. Introduction

Myelinated axons are critical in brain information processing because they play a central role in fast and reliable long range transmission of information between different brain areas. The defective myelin sheath can result in severe disturbances of motor and sensory functions. For fast transmission of information, the cable is sheathed by myelin that achieves two orders of magnitude increase and decrease of membrane resistance and capacitance, respectively. This indeed results in the two order of magnitude increase in spatial transmission speed whereas the order of time constant magnitude remains the same [1]. However, for long range communication, the signal needs to be amplified intermittently. For this, there exist the so-called nodes of Ranvier where the myelin sheath is absent and active ionic channels are present to amplify the signal.

Due to the presence of the nodes of Ranvier, a myelinated axon is not a uniform cable. Hence, it is easier to model separately the myelinated parts and the unmyelinated nodes of Ranvier. A node of Ranvier is small enough to be modelled by a single compartment. On the contrary, a myelinated part is described by a linear cable equation that is a parabolic partial differential equation. Due to the complexity associated with the continuous spatial variation in partial differential equations, a spatial discretization scheme is often adopted to get a system of ordinary differential equations (ODEs). For this, the compartment model based on finite volume or finite difference scheme was settled as a standard technique. For instance, the existing neuron simulators such as NEURON [2] and GENESIS [3] are based exclusively on the compartment model.

It is well known in computational physics that the spectral method including eigenfunction expansion techniques converges much faster than any other computational schemes for the problems with simple geometries [4]. Hence, if the spectral method is used, the same accuracy is achieved with a smaller number of approximate ODEs. In other words, the same

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number of ODEs will approximate the original PDE with a higher accuracy. Hence, the spectral method is better in finding a low order model with a reasonable accuracy as well. Indeed, the finite volume or finite difference method employs the local basis functions that are designed to represent the local variation of solution. It is hard for them to achieve with a small number of local basis functions a good approximation of the global spatial variation of solution. On the contrary, the spectral method uses global basis functions that are able to capture the global spatial features of solution with relatively small numbers of them.

The eigenfunction expansion of linear cable equations has been extensively studied in search for analytic solutions. Such results are well documented in [5]. However, these analytic results are valid only when the interaction with nonlinear elements such as soma and node of Ranvier is ignored. If such an interaction is considered, the entire problem becomes nonlinear so that an analytic solution is almost impossible to find. Hence, its real power in the reduced model and simulation of linear cables has not been examined. Since a myelinated part has a simple geometry, it seems reasonable to predict that the standard eigenfunction expansion can be applied to the cable as successfully as to the problems in computational physics. However, when time-varying boundary stimulation is severe, the standard eigenfunction expansion approach with the Galerkin truncation [6] of fast and stable high frequency eigenmodes is in general no better than the compartment approach [7]. Indeed, in most problems considered in computational physics, the boundary stimulation terms were absent. In these cases, zeroing fast and stable high frequency eigenmodes is justifiable since they converge quickly to their steady states that are quite small, if not zero, in most cases. However, when the external stimulation term is very severe as in a cable subject to a sequence of action potentials in a soma or a node of Ranvier, the deviations of high frequency modes from their very small steady states of the system without external stimulation introduce nonnegligible errors. To avoid this difficulty, we employed singular perturbation instead of the Galerkin truncation. In singular perturbation, the quasi-steady states of fast and stable high frequency modes that change subject to time-varying stimulations are used to capture the deviations. Indeed, singular perturbation was identified as a critical tool in a low dimensional controller design for the parabolic PDE systems that are externally excited by control inputs and disturbances [8,9]. Adopting singular perturbation, we demonstrated that eigenfunction expansion approach becomes as powerful in the reduced model and simulation of the neurons with few dendritic cables as in computational physics.

In this paper, for the reduced model and simulation of myelinated axon, we will apply the aforementioned eigenfunction expansion technique with singular perturbation to each myelinated part. For low order models, the proposed scheme achieved an order of magnitude accuracy improvement. Moreover, to achieve a given accuracy, the proposed scheme converged faster. Hence, the proposed scheme is superior than the conventional compartment model approach.

2. Methods

In this section, we consider a myelinated axon with 10 nodes of Ranvier as shown in Fig. 1. A myelinated part of the myelinated axon is described by the standard one-dimensional passive cable equation:

$$c_{\mathrm{m}}\frac{\partial v}{\partial \tau}=\frac{1}{r_{\mathrm{a}}}\frac{\partial^2 v}{\partial z^2}-\frac{1}{r_{\mathrm{m}}}v,$$

where

$$v=V-V_{\mathrm{rest}},$$

V is the membrane potential, V_{rest} is the resting potential of the cable, r_{a} is the axial resistance per unit length of the cable, r_{m} is the membrane resistance per unit length of the cable, c_{m} is the membrane capacitance per unit length of the cable.

For simplicity, we employ dimensionless time and space variables. For this, let $x=z/L$, where L is the length of a myelinated part. Then,

$$\tau_{\mathrm{m}}\frac{\partial v}{\partial \tau}=\lambda^2\frac{\partial^2 v}{\partial x^2}-v,$$

where the time constant τ_{m} and the dimensionless electrotonic length λ are defined by

$$\tau_{\mathrm{m}}=r_{\mathrm{m}}c_{\mathrm{m}},\quad \lambda=\sqrt{\frac{r_{\mathrm{m}}}{r_{\mathrm{a}}L^2}},$$

respectively. This equation has two parameters τ_{m} and λ. However, the dependence on τ_{m} can be eliminated by scaling the time variable as $t=\tau/\tau_{\mathrm{m}}$. Then,

$$\frac{\partial v}{\partial t}=\lambda^2\frac{\partial^2 v}{\partial x^2}-v.$$

Notice that the integration of this equation over the unit time interval in t corresponds to that of the original equation over the time interval τ_{m} in τ. Notice that the solution in the original time and space coordinate can be readily recovered.

For $i=1,\ldots,10$, the nonterminal myelinated parts are described by

$$\tau_{\mathrm{m}}\frac{\partial v_i}{\partial t}=\lambda^2\frac{\partial^2 v_i}{\partial x^2}-v_i, \tag{1}$$

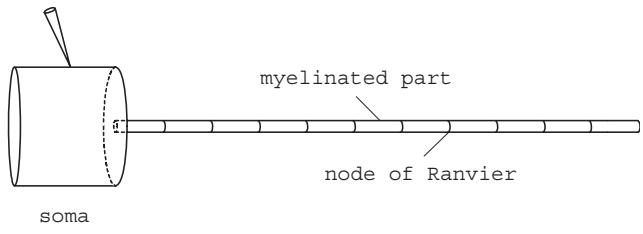

Fig. 1. Myelinated axon with soma.