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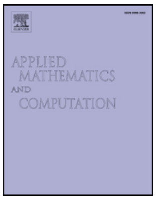

On the dynamics of axonal membrane: Ion channel as the basic unit of a deterministic model

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ABSTRACT

Here we propose a deterministic model for computing the electric potential of axonal membrane, based on simplifications of the properties of its ion channels. The model can reproduce typical dynamic behaviors, like passive (exponential) decay, generation and propagation of action potentials, and frequency adaptation. Numerical results are compared to theoretical analyses and experimental data, showing good agreement.

1. Introduction

It is possible to study the Nature in a wide variation of scales: from the nanoscale of protons and neutrons to the gigantic dimensions of stars and galaxies. Each scale has its purpose: there is no sense in trying to understand the atomic nucleus in an astronomical extent and it is impractical to explain astronomical events in typical atomic lengths. However, the trouble is that, sometimes, the big and the small are not easy to separate. Biology is a scientific domain in which macroscopic and microscopic scales overlap and interact in subtle and puzzling ways.

The human brain is an example of a biological system in which macroscopic and microscopic scales are strongly connected [1]. For instance, it is impressive to realize how a small amount of some drugs can lead to a striking change in human behavior, making evident that tiny molecules can produce visible effects.

In this work, we propose a way of determining the electric potential of (macroscopic) axonal membrane of neurons, by considering (microscopic) ion channels as the building blocks. Thus, the ion channel is considered the basic unit of our model. We show that several dynamical behaviors can be observed, like passive decay, action potential propagation, and firing frequency adaptation.

To construct our model, we looked at Markov models [2,3], also called kinetic schemes in some contexts [4,5], investigations based on cellular automata [6–10], transfer-function models [11], and the original work by Hodgkin and Huxley [12]. Also, we analyzed studies on ion channels [13–15].

Our model, formulated in terms of a cellular automaton, has two main features: 1) each channel has memory, meaning that the next state depends not only on the current one, but also on the history of its activation; 2) the model is fully deterministic: each state is completely determined from a set of deterministic rules, and the membrane potential is calculated

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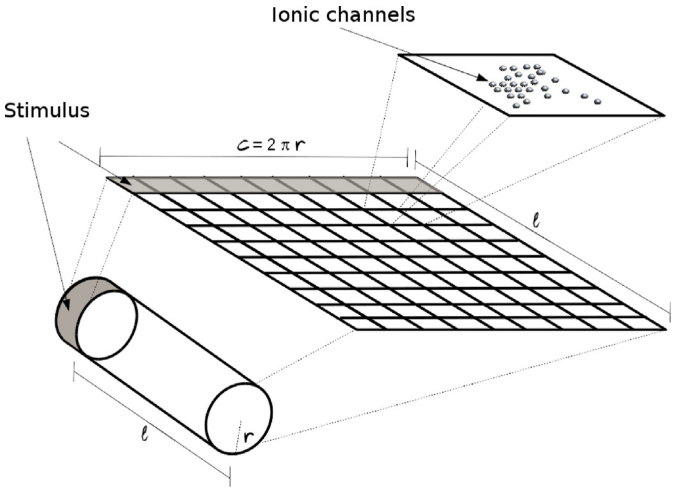

Fig. 1. Geometrical description of the axon.

from a deterministic function. The results obtained from numerical simulations show good agreement with other theoretical investigations [12,16] and data obtained from real neurons [17,18].

This manuscript about neuronal dynamics is structured as follows. In Section 2, the model of axonal membrane written in terms of deterministic rules is described. In Section 3, the results of numerical simulations in several conditions are compared to theoretical works and experimental data. In Section 4, the conclusions are stressed.

2. The model of axonal membrane

The proposed model is focused on the relation between the neuron behavior and the channels in its membrane. In real neurons, action potential results from the opening and closing of certain groups of ion channels in the cell membrane. Each channel has a small contribution to the overall dynamics, altering the local potential. It is the collective behavior of all ion channels that determines the membrane potential, by changing ion concentrations in the cell interior [5,19]. Also, most of the ion channels in the neuronal membrane are mainly permeable to only one kind of ion, and much less to others types [20,21]. Thus, to generate an action potential, there must be a coordination among opening and closing of ion channels generated by their own interactions. The timing properties of each channel influence the shape and the frequency of the action potential.

In our model, the axonal membrane is considered as a grid, as shown in Fig. 1. The grid is formed by x rows and y columns. The rows represent the longitudinal direction; the columns, the transverse direction. Each square in the grid corresponds to a membrane patch. Inside each patch there is a set of ion channels. The patch size must be chosen to be small enough so that all ion channels in it are in the same electric potential. Hence, the size of the patch must be smaller than the electrotonic length and, then, the geometric position of each channel inside the square becomes irrelevant. Here, each patch has a geometric size of 100μm by 100μm. The first two columns in the grid are the so called axon initial segment [22], at the axon hillock. Such a region seems to play a definite role in the generation of the action potential in real neurons [22]. Therefore, these first two columns is the region where the stimulus is usually applied in our simulations related to action potential.

Like space, time is also a discrete variable in our model. Each iteration is equivalent to 1 μs of real time. This choice gives a good time resolution to model the axonal dynamics, without being computationally costly.

In this model, each ion channel presents specific features, which are listed below:

Type: Here, two types are used: voltage-gated ion channels and leak channels. The ions considered in this work are sodium and potassium.

State: At each iteration, each channel must be in one of the following states: open, closed, or inactivated.

Open threshold: This is the tension limit at which the channel opens.

Time to close: This is the number of time steps (iterations) that a channel stays in the open state before it closes.

Delay: This is the number of iterations that the channels have to wait before opening after the open threshold having been reached.

Inactivity period: This is the duration (in iterations) of the inactivated state.

Here, the voltage-gated sodium channel has three states: open, closed, and inactivated. It starts in the closed state and it opens when the tension of the membrane patch where it is embedded reaches a specific threshold (in our simulations, this threshold value is equal to −55 mV). There is also a delay for the channel opening (chosen to be 2 μs). After this delay,