Computers in Biology and Medicine 43 (2013) 693–698

Contents lists available at SciVerse ScienceDirect

Computers in Biology and Medicine

journal homepage: www.elsevier.com/locate/cbm

A mathematical based calculation of a myelinated segment in axons

Hamidreza Namazi *, Vladimir V. Kulish

School of Mechanical and Aerospace Engineering, Nanyang Technological University, Singapore

ARTICLE INFO

Article history:
Received 23 June 2012
Accepted 18 March 2013

Keywords:
Neuron
Axon
Action potential
Diffusion
Length
Myelinated segment

ABSTRACT

The brain is a complicated system that controls all of the body's actions and reactions by receiving and processing different stimuli and producing the proper responses. The brain accomplishes this task using various sensory elements such as neurons. The axon is the most important element of the neuron in terms of signal generation and propagation. Although much effort has been made studying the characteristics of the axon, there is no research that focuses on measuring the length of this element from a mathematical point of view. In this paper, we propose for the first time a new mathematical model of the generation of action potentials in the axon. Using this model and the diffusion phenomenon in axons, we propose a characteristic length for the myelinated segments in axons. This mathematically calculated value is corroborated by comparison with values measured by biologists.

1. Introduction

The brain is the most complex organ in the human body and controls all of the body's actions based on various stimuli received through the nervous system. Any stimulus stronger than the threshold stimulus is translated by a number of sensory neurons that generate information about the stimulus through the frequency with which they fire action potentials. After the action potential has been generated, it travels through the neural network to the brain. In various sections of the network and in the brain, integration of the signals occurs. Different areas of the brain respond depending on the type and location of the stimulus. Then, the brain generates and transmits signals that produce responses.

The axon is the most important element of the neuron in terms of signal generation and propagation.

Over many years, there have been numerous studies on the characteristics of axons. Some researchers have tried to measure the different sizes of axons. For example, Broser et al. developed a new method to quantify axon length in populations of labeled neurons. In their research, they analyzed high-resolution images to determine the length of rat axons using specifically developed image-processing algorithms. The results of their study agreed very well with manually measured axon lengths [1]. In another study, Yong Tang and Jens R. Nyengaard proposed a reasonably fast, efficient, and unbiased stereological method to obtain estimates of the volumes and total lengths of myelin fibers in human brain white matter [2].

Some scientists have investigated the relationships between the different geometrical characteristics of axons. For instance, using a micrometer and Dogger general digital analyzer, Ibrahim et al. measured external myelin sheath diameter and intermodal length in adult rats and, through the use of statistical analyses, they suggested a linear relation between these two measures [3]. In a similar study, Fazan et al. claimed that the relation between myelin area and axon diameter in the aortic depressor nerve of spontaneously hypertensive rats is altered [4], see also [5]

In an interesting study, Velumian et al. visualized cytoplasmic diffusion within living myelin sheaths of CNS white matter axons using microinjection of the fluorescent dye Lucifer yellow. These authors claimed that their results could be relevant to MRI studies of CNS white matter and CNS repair/regeneration strategies [6].

Despite some advances in studies related to the characteristics of axons, there has been less progress in the modeling of the geometrical dimensions of human axons from a mathematical point of view. However, contemporary developments in physics and mathematics enable us to work on this issue.

This paper introduces a new mathematical model of the generation of single action potentials in the axon, and, using this model and employing the diffusion phenomenon in axons, we define a characteristic length which stands for the length of the myelinated segments of axons.

2. Impulse generation and propagation mechanisms in the axon

An axon, or nerve fiber, is a long, thin process of a neuron that typically conducts electrical impulses away from the neuron's cell body.

* Corresponding author. Tel.: +6593708457.
E-mail address: m080012@e.ntu.edu.sg (H. Namazi).

0010-4825/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.compbiomed.2013.03.005

In vertebrates, axons are enclosed in an insulating myelin sheath formed by special neuroglia cells (Fig. 1). The myelin sheath increases the speed of impulse transmission and also prevents the ionic gates in those parts of the axon from opening and exchanging their ions with the outside environment.

There are periodic gaps between the myelin sheath segments known as the nodes of Ranvier. At these uncovered areas of the axonal membrane, the ion exchange that is necessary for the production of action potentials occurs.

An inactive or resting neuron actively pumps sodium ions (Na^+) out the cell and potassium ions (K^+) into the cell. However, the plasma membrane is more permeable to K^+ than Na^+ ions, and thus, K^+ ions diffuse out of the neuron. This diffusion results in excess positively charged ions outside the neuron's membrane and excess negatively charged ions inside the neuron. This unusual distribution of electrical charges across the plasma membrane polarizes the membrane, and this condition is known as the resting potential; typical resting potentials are between –60 and –70 mV (Fig. 2). A potential is the difference in electrical charge between two sites. The polarization of the neuron's membrane does not change as long as the neuron is inactive.

When the neuron receives an incoming stimulus, it exhibits an all-or-none response. The neuron either produces an impulse or fails to respond. The weakest stimulus that will activate a neuron is called a threshold stimulus. When a neuron is activated by a stimulus, its plasma membrane instantly becomes permeable to Na^+, and these ions quickly diffuse into the neuron. The inward flow of Na^+ causes positive and negative ions to be equally abundant on either side of the plasma membrane. Thus, there is no net electrical charge across the membrane; i.e., the plasma membrane is now depolarized. This sudden depolarization is the nerve impulse, or action potential. The wave of depolarization then flows along the myelinated axon.

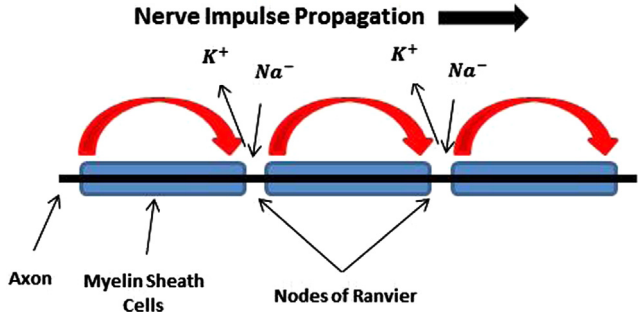

Fig. 1. Schematic structure of a typical axon.

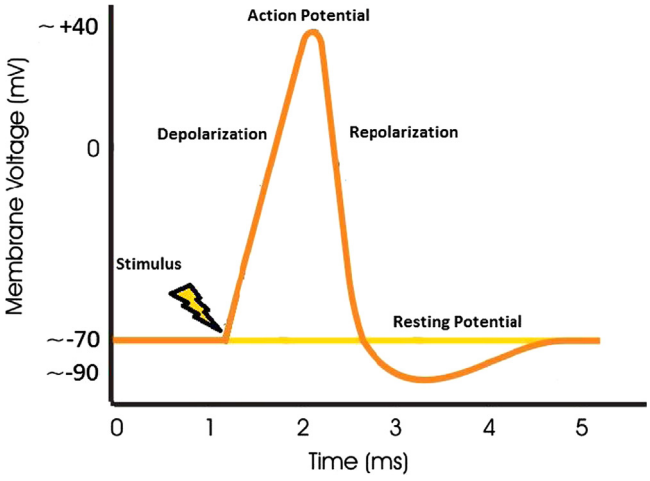

Fig. 2. Action potential initiation in a neuron.

Immediately after depolarization, K^+ ions diffuse outward to reestablish the resting potential of the membrane by reproducing the excess of positive charges outside, and excess negative charges inside, the membrane; thus, the neuron membrane is repolarized. Next, Na^+ is pumped out, and K^+ is pumped into the neurons to reestablish the resting-state distribution of ions. When this is accomplished, the neuron is ready to respond to another stimulus. Depolarization and repolarization are accomplished in approximately 1/1000 of a second.

3. Model of single action potential generation

Here, we analyzed the characteristics of the axon from a mathematical point of view. To do so, we first needed a mathematical model of the action potential.

We introduce a time lag term that takes care of the lag between the occurrence of the stimulus and the rise of the subsequent action potential. Thus, the constitutive relation to be coupled with the conservation equation must be the following:

$$\Psi(x,t+\tau) = -D\frac{\partial V}{\partial x}(x,t) \tag{1}$$

where $\partial V/\partial x$ on the right hand side of Eq. (1) is the direct result of the external influence (i.e., the stimulus), and the term τ is the time lag that ensures the paradox of instantaneous propagation does not become a factor.

Thus, the quantities involved in Eq. (1) are written for two different instances of time. To bring these physical quantities into the same time instance, it is necessary to expand the left side of Eq. (1) with Taylor's series, while keeping in mind that the lag time is small compared with the transient time of the process; thus, we can neglect those terms of the expansion whose orders are larger than one; i.e.,

$$\Psi(x,t) + \tau\frac{\partial \Psi}{\partial x}(x,t) \cong -D\frac{\partial V}{\partial x}(x,t) \tag{2}$$

which is Fick's law with a finite lagging time.

Now, we need to couple the new constitutive relation expressed by Eq. (2) with the conservation equation. To do so, let us find the derivative of Eq. (2) with respect to x. We thus obtain

$$\Psi_x + \tau\frac{\partial \Psi_x}{\partial x} \cong -DV_{xx} \tag{3}$$

from the conservation equation, it follows that:

$$\Psi_x = -V_x + f(x,\ t) \tag{4}$$

where $f(x,\ t)$ is the source function.

Upon substituting (4) into (3), we obtain

$$\tau\frac{\partial^2 V}{\partial t^2} + \frac{\partial V}{\partial t} = D\frac{\partial^2 V}{\partial x^2} + f(x,t) + \tau f_t(x,t) \tag{5}$$

Denoting

$$S(x,t) = f(x,t) + \tau f_t(x,t) \tag{6}$$

We have

$$\tau\frac{\partial^2 V}{\partial t^2} + \frac{\partial V}{\partial t} = D\frac{\partial^2 V}{\partial x^2} + S(x,t) \tag{7}$$

where $\tau = D/c^2$. The speed of propagation, which is a finite quantity, denoted by c. In fact, c is the speed of the impulse travelling through the neuron. The diffusivity term, D, is related to the resistance of the neuron to the electrical impulse; this is the property of the neural tissue and will dampen the impulse as it travels over the nerve.