Examine of electrical conduction processes in blood vessels by cable theory

Natela Zirakashvili
I. Vekua Institute of Applied Mathematics of Iv. Javakhishvili Tbilisi State University, Georgia
natzira@yahoo.com

Abstract**:** *Electrical conduction processes in the vasculature have traditionally been described using cable theory, i.e., locally induced signals (membrane potential) decaying passively along the arteriolar wall. The decay is typically quantified using the length-constant, , derived from cable theory. While cable theory provides a useful framework for modeling electrical conduction in biological tissues, its assumptions are often violated in the context of small arteries and arterioles. Arterioles are composed of at least two cell layers: an inner endothelial cell (EC) layer and one or more outer smooth muscle cell (SMC) layers. These layers are connected by myoendothelial gap junctions (MEGJ), allowing electrical signals to pass between them. This work discusses arterioles with two cell layers and studies the change in membrane potential in the EC and SMC layers. The corresponding stationary problems are posed and solved analytically by the method of separation of variables. Numerical modeling of membrane potential propagation is performed using MATLAB software. Visualizations include isopotential contours, 2D and 3D graphs of over space and time, and plots of variation along the vessel and over time.*

Keywords: *CABLE EQUATION, MEMBRANE POTENTIALl, ARTERIOLE, ENDOTHERIAL CELL LAYERS, SMOOTH MUSCLE CELL LAYERS, SEPARATION VARIABLES METHOD*

1. Introduction

Membrane potential V_m plays a crucial role in vascular contractility irrespective of mechanical or chemical stimulus. V_m is determined by the activity of ion channels and each cell in turn shares information with neighboring cells via gap junctions. This direct exchange of information presumably enables multiple vessel branches to coordinate their responses. Such coordination would, in theory, allow arterial structures to effectively regulate blood flow [1-3]/

Arterioles consist of at least two cell layers—an endothelial cell (EC), and one or more smooth muscle cell (SMC) layers that are coupled by myoendothelial gap junctions (MEGJ). ECs are long and flat and are oriented along the vessel length axis. SMCs are spindle-shaped and wrap around ECs in a perpendicular arrangement. ECs and SMCs were modeled in an overlapping pattern, as shown in Fig. 1.

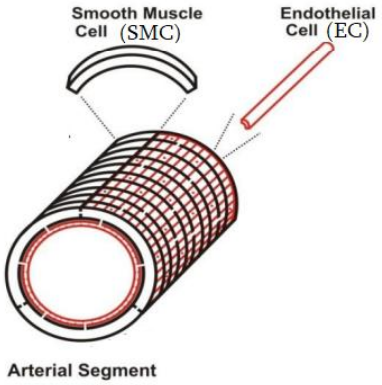


Figure 1 *Schematic drawing of a vessel segment. The vessel is composed of two cell layers, endothelial cells (ECs) innermost with smooth muscle cells (SMCs) around. ECs are oriented along the vessel axis, while SMCs wrap around ECs perpendicularly.*

The current work discusses two cell-layered (EC and SMC cell layers) arterioles and studies the change in membrane potential in these layers. Numerical modeling of membrane potential propagation for a one-dimensional model of a two-cell-layered cylindrical arteriole, in the absence of current at the beginning and end of the cable (arteriole) is performed using MATLAB software. Numerical results are obtained and corresponding membrane isopotential contours, 2D and 3D graphs are presented.

2. Theoretical aspects

2.1. Problem formulation and principal formulas

Spread of V_m changes in biological cablelike structures is usually described using cable theory. One of the main problems of cable theory is the calculation of membrane potential. The theory of cables, developed in recent decades, is older than the cable equation itself, being a variation of the equations developed by Lord Kelvin to model the propagation of electrical signals from underwater telegraphs. The cable theory was originally applied to conducting potentials in the axon, for example, by Hodgkin and Rushton. It has been applied to neurons, arrays of cells [4] and to blood vessels [5,6].

The passive cable equation will be written as follows:

$$\tau_m \frac{\partial V(x,t)}{\partial t} = \lambda^2 \frac{\partial^2 V(x,t)}{\partial x^2} - V(x,t) \qquad (1)$$

where $V := V_m$ is the membrane potential, $\lambda = \sqrt{\frac{r_m}{r_l}}$ is the constant of the space (length) of the passive cable equation which determines the distance along the cell at which the injected potential decreases by factor e, and $\tau = r_m c_m$ is a time constant, it determines the length of time over which the injected potential decreases by factor e. r_m is membrane resistance, c_m is membrane capacity , and r_l is the resistance of the cell cytoplasm per unit length. Space and time constants are useful parameters used to measure and characterize specific properties of excitable tissues.

An important set of basic assumptions is usually made when applying cable theory to small blood vessels (for a complete description, see Holt : Holt, G. 1998. A critical reexamination of some assumptions and implications of cable theory in neurobiology. PhD thesis, California Institute of Technology, Pasadena, CA.):

1. Intra- and extracellular spaces are one-dimensional and homogeneous.
2. Electrotonic conduction is Ohmic (follows Ohm's law).
3. Membrane resistance is independent of the resting potential.
4. Ion channel conductances are time- and voltage-independent.
5. Ionic concentrations are constant.

2.2. Problem statement and solution

Consider a cylindrical two cell-layered arteriole of length L. Let us solve the passive cable equation (1) with the following boundary and initial conditions: 1) there is no current flowing into the cable (at the beginning of the cable) and out of the cable (at the end of the cable), and 2) at the beginning of time interval, the current is a function only of the spatial coordinate x of the cable. Thus, the boundary and initial conditions will be written as follows:

$$\begin{aligned} &\text{For } x = 0: \; V_{,x}(x,t) = 0, \\ &\text{For } x = L: \; V_{,x}(x,t) = 0, \end{aligned} \qquad (2)$$

$$\text{For } t=0:\ V(x,0)=f(x). \tag{3}$$

Using the method of separation of variables and considering the boundary (2) and initial (3) conditions, we will obtain the following expression:

$$V(x,t)=\frac{2}{L}\frac{L^2}{2}+\frac{2}{L}\sum_{n=1}^{\infty}\left[\frac{L^2}{\pi n}\sin(\pi n)+\left(\frac{L}{\pi n}\right)^2(\cos\pi n-1)\right]\cos\left(\frac{\pi nx}{L}\right)e^{\left(1-(\lambda\pi n/L)^2\right)t/\tau_n}$$

$$=L+2L\sum_{n=1}^{\infty}\left(\frac{1}{\pi n}\sin(\pi n)+\frac{1}{(\pi n)^2}(\cos\pi n-1)\right)\cos\left(\frac{\pi nx}{L}\right)e^{\left(1-(\lambda\pi n/L)^2\right)t/\tau_m},$$

$$V_{,x}(x,t)=-2\sum_{n=1}^{\infty}\left[\pi n\left(\frac{1}{\pi n}\sin(\pi n)+\frac{1}{(\pi n)^2}(\cos\pi n-1)\right)\sin\left(\frac{\pi nx}{L}\right)e^{\left(1-(\lambda\pi n/L)^2\right)t/\tau_m}\right].$$

3. Numerical simulation

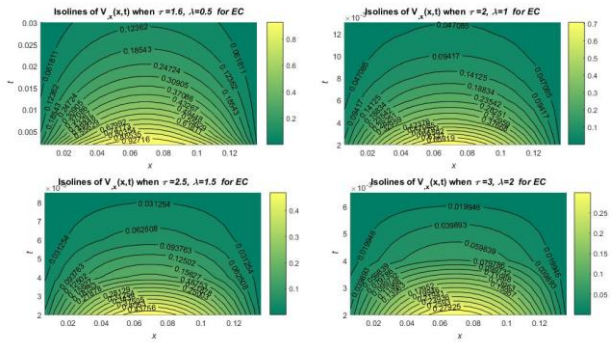
Simulations were performed for a two-layered arteriole (EC and SMC) with various values of τ and λ. Example parameter sets:

- $\tau=1.6ms,\ \lambda=0.5mm$
- $\tau=2ms,\ \lambda=1mm$
- $\tau=2.5ms,\ \lambda=1.5mm$
- $\tau=3ms,\ \lambda=2mm$.

Arteriole length: $L=750\mu m=0.75mm$; spatial discretization: $\Delta x=6\mu m=0.006mm$; temporal discretization: $\Delta t=0.005ms$ was used. Numerical values of membrane potential change $V_{,x}$ for various fixed temporal τ and spatial λ constants and obtained during the variation of x (from $0.006mm$ to $0.136mm$ for EC $0.304mm$ for SMC) and t (from $0.01ms$ to $0.03ms$). are obtained.

In practice, a system of contours (isolines) is often used to analyze the measurement results. For arterioles , some contours of membrane potential change $V_{,x}$ for the plane area in the vector field of space (length) x and time t are presented.

(a)



(b)

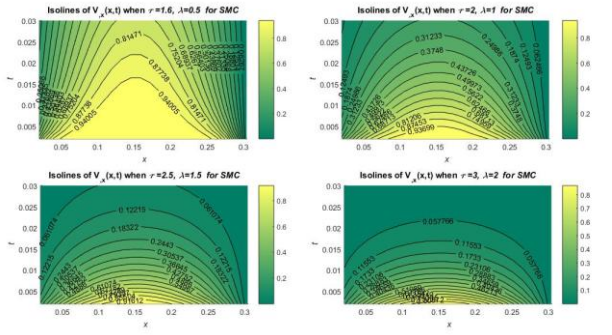
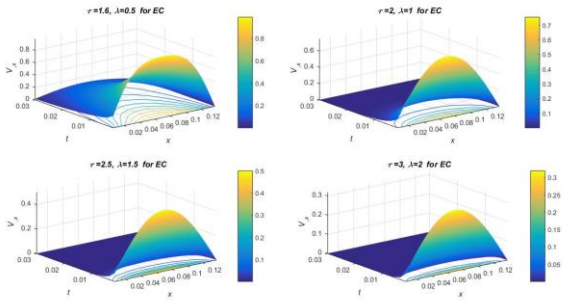


Figure 2 *Membrane isopotential contours for different fixed values of time and space constants (a) for the endothelial cellular (EC) layer, (b) for the smooth muscle cellular (SMC) layer.*

(a)



(b)

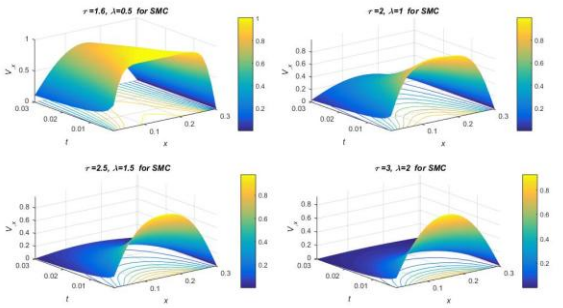
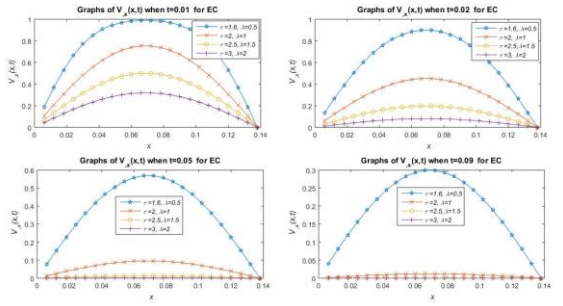


Figure 3 *3D graphs of membrane potential change $V_{,x}$ distribution in the x , t vector field for different fixed values of time and space constants (a) for the endothelial cellular (EC) layer, (b) for the smooth muscle cellular (SMC) layer.*

(a)



(b)

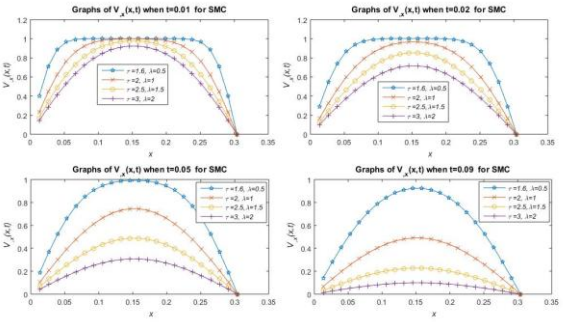


Figure 4 *Graphs of variation of membrane potential $V_{,x}$ along x for different fixed values of time τ and space λ constants and four fixed values of t , (a) for the endothelial cellular (EC) layer, (b) for the smooth muscle cellular (SMC) layer*

(a)

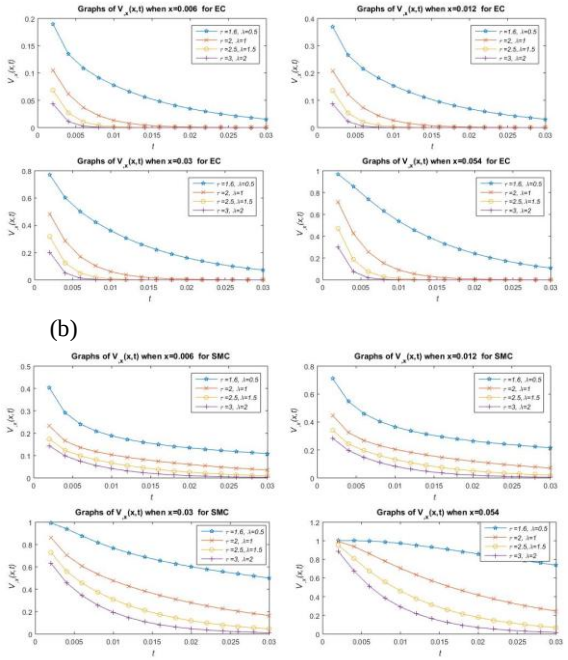


Figure 5 *Graphs of variation of membrane potential $V_{,x}$ along t for different fixed values of time τ and space λ constants and four fixed values of x, (a) for the endothelial cellular (EC) layer, (b) for the smooth muscle cellular (SMC) layer*

Results show that the change in membrane potential $V_{,x}$ is smaller in the EC layer than in the SMC layer, indicating poorer current propagation in SMCs.
Finally, the research has not been completed and continues to study and solve various problems in this area as far as possible.

4. Conclusion

The main results presented in this paper can be formulated as follows:

- The change in membrane potential in the endothelial cell layer and the smooth muscle cell layer is studied using the passive one-dimensional cable equation (endothelial cell (EC) and smooth muscle cell (SMC) layers), for a two-cell-layered arteriole.

- For a one-dimensional model of a two-cell-layered cylindrical arteriole, in the absence of current at the beginning and end of the cable, numerical modeling is carried out using the software MATLAB. Numerical results of the change in membrane potential are obtained, based on which membrane isopotential contours are constructed for a flat area in the vector field of length x and time t. Some 2D and 3D graphs are also built.

- From the obtained numerical results and corresponding graphs, it can be seen that the change in membrane potential $V_{,x}$ is smaller in the EC layer, than in the SMC layer, which is caused by poor current propagation in the SMC layer.

Cardiovascular diseases continue to be the foremost cause of mortality globally. It shall be noted, that despite of extensive research over many years, the propagation of membrane potential in blood vessels has not been comprehensively explored, therefore, its study remains an actual topic of much modern scientific research. This paper aims to study changes in membrane potential in blood vessels using the cable equation. Finally, we are continuing our research and will study and solve some of the problems in this field to the fullest extent possible.

5. References

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