Mathematical model of neuronal membrane mechanical deformations under the influence of an electric pulse

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Abstract. Mechanical deformations of neuronal membrane occur when exposed to an electrical pulse. A one-dimensional mathematical model of such deformations of a cylindrical cell is proposed, based on the fluid dynamics equations and the Lippmann equation connecting electric effects with the membrane strength. The model qualitatively reproduces experimentally observed effects of cell membrane mechanical deformations evoked by both an action potential moving along axon and an electric pulse injected through electrode.

1. Introduction
Electrical processes play a major role in the activity of brain cells, neurons, involving opening and closing ion channels, transmitting information from one neuron to another, etc. The main information is transmitted along neuronal branches by means of electrical pulses, named action potentials or spikes. The ionic channels that provide neuronal excitability are governed by voltage. According to the classical theory [1], the neuronal excitability is described by a diffusion equation coupled with highly nonlinear ordinary differential equations. This system gives solutions in a form of electrical pulses approximately described as autowave processes. Experiments revealed that a neuron generating an electrical pulse also changes its shape. For example, an electrical pulse passing through an axon is accompanied by small oscillations of the axonal membrane [2]. This phenomenon is related to other processes taking place in neurons when exposed to pulses [3] or osmotic forces [4]. However, the mechanism of these membrane deformations is fully understood. Hence, a mathematical model of the dynamics of the deformations is unknown.

It is highly likely that the electrical potential changes mechanical properties of the membrane, which, in turn, changes its shape. This is reflected by Lippmann's equation linking the membrane's electrical potential and surface tension. This equation provides the basis for a mathematical model describing the mechanical displacement of the membrane when the neuron is exposed to an electric pulse.

2. Mathematical model and numerical scheme
A one-dimensional model is based on the fluid dynamics equations for a water-based electrolyte medium surrounded by an elastic membrane of a modeled neuron. We consider a cylindrical branch of length L and radius R, shown in Figure 1. The membrane is initially strengthened by the osmotic pressure not fully balanced by the hydrostatic pressure.
The continuity equation for the incompressible fluid, written in cylindrical coordinates, takes the form:

$$\frac{1}{r} \frac{\partial (r V_r)}{\partial r} + \frac{\partial u}{\partial x} = 0$$  \hspace{1cm} (1)$$

Where $V_r$ is the velocity projection on r-axis, $u$ is the projection of the velocity on the x-axis.

After averaging across the radius, the equation for the average speed $\bar{u}$ and the time variable radius $R(t)$ becomes:

$$\frac{2 \dot{R}}{R} + \frac{\partial \bar{u}}{\partial x} = 0$$  \hspace{1cm} (2)$$

The momentum balance equation is as follows:

$$\frac{\partial \bar{u}}{\partial t} + \frac{1}{\rho} \frac{d p_i}{dx} = 0$$  \hspace{1cm} (3)$$

Where $p_i$ is the internal pressure, which, taking into account its balance with the osmotic pressure, is equal to the membrane tension, i.e.

$$p_i = \Delta p_o$$  \hspace{1cm} (4)$$

According to [4], the membrane tension is calculated as follows:

$$\Delta p_o = E \frac{R - R_0}{R_0^2}$$  \hspace{1cm} (5)$$

Where $E$ is the module of the membrane elasticity, $R_0$ is the unperturbed radius. Taking all transformations into account, the following system of equations is obtained:

$$\begin{cases} 
\frac{\partial \bar{u}}{\partial t} + \frac{1}{\rho} \frac{d p_i}{dx} \left( \frac{E(R - R_0)}{R_0^2} \right) = 0 \\
\frac{2 \dot{R}}{R_0} \frac{\partial \bar{u}}{\partial x} = 0
\end{cases}$$  \hspace{1cm} (6)$$

This is a hyperbolic system of transport equations. The speed of propagation of the disturbances is:

$$a = \sqrt{\frac{E}{\rho R_0}}$$  \hspace{1cm} (7)$$

The Lippmann equation which explains membrane perturbations in electrical field reads

$$\frac{\partial \gamma}{\partial V} = -q$$  \hspace{1cm} (8)$$

Where $\gamma$ is the surface tension, $V$ is the electric potential of the membrane, and $q$ is the excess mobile charge. In our consideration, the voltage is proportional to the elasticity modulus with some coefficient.
Free surfaces are specified as boundary conditions at the ends of the cylinder. Two tasks with different electrical pulses have been considered.

1. The membrane response to a triangular pulse $E(t, x)$ moving at 1 m/s. This case corresponds to the experiment with an action potential travelling along an axon [2]. The voltage profile of the action potential is approximated with the triangle.

2. The membrane response to a short electrical pulse, duration 10 ms, localized within a segment of the neuron. This case corresponds to the experiment with a cell stimulated through an electrode [3].

The second experiment [3] implies dissipative processes affecting the response, which are due to the viscosity of the fluid and the intracellular matrix. Therefore, for task 2, the viscosity was added to the momentum conservation equation (2):

$$\frac{\partial \bar{u}}{\partial t} + \frac{1}{\rho} \frac{\partial}{\partial x} \left( E(R - R_0) \right) - \frac{\partial^2 \bar{u}}{\partial x^2} = 0$$  \hspace{1cm} (9)

The mathematical model was coded in the Delphi7 environment. A numerical scheme has been obtained with: (i) factorization according to physical processes, transport and dissipation; (ii) an explicit first-order Godunov-like numerical scheme for the hyperbolic part of the equations; and (iii) a Thomas algorithm-based implicit numerical scheme for the parabolic part. The Godunov-like scheme has been obtained through Riemann invariants as the linear combinations of the velocity and radius. Boundary conditions were specified as free surfaces. The numerical scheme written in terms of the central differences denoted by brackets is as follows:

$$\left\{ \frac{\partial \bar{u}}{\partial t} + \frac{1}{\rho} \frac{\partial \left( E(R - R_0) \right)}{\partial x} \right\} = \sqrt{\frac{E}{\rho R_0}} \frac{\Delta x}{2} \left[ \frac{\partial^2 \bar{u}}{\partial x^2} \right]$$

$$\frac{2}{R_0} \frac{\partial R}{\partial t} + \frac{\partial \bar{u}}{\partial x} = \sqrt{\frac{E}{\rho R_0}} \frac{\Delta x}{2} \left[ \frac{\partial^2 R}{\partial x^2} \right]$$  \hspace{1cm} (10)

### 3. Results

**Task 1.** The effect of electrical pulses on the cell is the short-term deformation of the cell shape. Consider the task 1. Based on the parameters of the experiment [2], the speed of propagation of disturbances is about 0.73 m/s, calculated with eq.(7) and the following parameters: the density of 1000 kg/m$^3$ and undisturbed modulus of elasticity 0.0001 g/ms$^2$. Task parameters also include: the unperturbed radius 190 mkm, initial radius 200 mkm, neuron length 5000 mkm.

![Figure 2](image-url)  \hspace{1cm} *Figure 2. Task 1. Evolution of the radius deflections at one location of the cylindrical neuron, evoked by a triangular electric pulse that affects the membrane elasticity: experiment [2] (left panel) and simulation (right).*
The displacement of the membrane evoked by the triangular pulse of $E$ at a particular point of neuron is shaped as a positive-negative pulse (Figure 2). The cell radius is initially increased in concert with the passing pulse, and then a negative pulse of smaller amplitude, but longer in time. The model reproduces qualitatively this shape. The correlation of the response with the input moving pulse suggests that the response is a wave; however the spatial profiles reveal that the shape of the response gradually changes. Figure 3 shows the profiles of the elasticity modulus and the membrane deflection at different time moments. The complex moves to the right. Membrane deformation strictly follows the changes in the modulus of elasticity. The increase of the elasticity modulus increases the radius. Since the speed of perturbations propagation $\alpha$ is less than the pulse speed, the secondary pulse of the opposite sign moves slower than the first one, as seen from comparison of the left and right panels in figure 3.

**Figure 3.** Task 1. Spatial profiles of the modulus of elasticity $E$ and the deviation of radius $R$ at various moments of time.

*Task 2.* A short electric pulse, duration 10 ms, is applied on a central segment of a neuron. The geometry of this task is characterized by an initial radius 10 mkm, unperturbed radius 9.9 mkm and neuron length 50 mkm. Simulation was performed with the additional viscosity of 2000 $\mu$m$^2$/ms and the undisturbed value of $E$ equal to $2 \cdot 10^{-8}$ g/ms$^2$. Similar to the experiment [3], two variants of pulses have been set (Figure 4). The first is the decreasing value of the membrane elasticity module $E$, which results in weakening of the membrane and the increase of the radius. In the second variant, $E$ increases and the neuron contracts. In both cases, after the end of the pulse, the membrane returns smoothly to its initial position. For points in the center, deformation of the membrane and its return to initial position after the end of the impulse occur monotonously (data not shown). However, on the periphery, the membrane deviation trace is more complex. As soon as the pulse ends, the membrane starts to return to its original position and the liquid is pushed out of the periphery, which causes a local peak.
Figure 4. Task 2. Membrane disturbance evoked by the electric pulses of various signs, positive (solid line) and negative (dashed line): experiment [3] (left panel) and simulation (right).

Concluding, the proposed model qualitatively reproduces the experimentally observed effects of cell membranes mechanical deformation, evoked by both the natural action potential and the artificial electric pulse. Further parametric analysis of the mathematical model is expected to provide certain predictions for experimental validation of the theory.

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