SIMULATION OF NEURAL IMPULSES PROPAGATION BLOCK BY HIGH-FREQUENCY SIMULATION

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Abstract

Electrical stimulation of a neural fibre is an alternative treatment of many neurological diseases, where conventional treatment procedures have undesirable side effect. Development of electrical stimulation technique suitable for reversible block propagation of pathological neural impulses is a challenging task. In this article, we have analyzed possibility of neural impulse propagation blocking by computer simulation. We have modeled neural fibre using partial differential equation and solved the model in Matlab. We have demonstrated that a high frequency stimulation has potential to disrupt pathological neural propagation.

1 Introduction

Many neurological diseases are characterized by increased neuronal activity that results in undesirable sensory or motoric effects, such as pain, abnormal muscle activity, spasticity, or tremor. Conventionally used treatment methods involve surgical and pharmacological procedures that are often accompanied by irreversible changes and side effects. An electrical stimulation that electrically blocks propagation of the neural activity is a perspective alternative treatment.

Up today, various types of electrical stimulation techniques have been developed, utilizing different mechanism of action to achieve expected clinical goal. Surface stimulation is useful for muscle strengthening, localized stimulation of small muscle groups is required to restore some motor and sensory function. Conventionally, stimulation of a nerve fibre increases its neural activity. Therefore, inhibition of neural activity, desirable for pain and spasticity reduction, is usually achieved trough neurophysiological feedback pathways. Possibility to block the undesired activity propagation by electrical stimulation is a challenging alternative.

Electrical stimulation of a nerve fibre commonly initiates two action potentials that propagate in opposite directions from the stimulated region. Impulse propagation can be stopped by eliciting a unidirectionally propagated collision impulse or by the high frequency (HF) alternating current stimulation [1] – [4]. Eliciting of collision impulse requires special (tripolar) arrangement of stimulation electrodes [5]. It has been demonstrated experimentally that high frequency high amplitude stimulus can also result in reversible conduction block [2], [3]. Mathematical modeling and computer simulation are useful in deeper understanding of this phenomenon.

This paper presents simulation of the effect of an alternating current stimulus on the neural impulse propagation. The neural fibre is modelled by partial differential equation (PDE) based on Fitzhugh-Nagumo model [6], [7]. The system of PDE is numerically solved by means of Matlab function *pdepe*.

2 Neural fibre model

Mechanism of neural action potential propagation can be investigated using segments of lumped circuit model or using partial differential equations. Local segment of different nerve fibre are modeled using particular local model, e.g. Hodgkin-Huxley (HH) model of unmyelinated nerve fibre [8], Fitzhugh-Nagumo model [6], [7], Frankenhaeuser-Huxley model [9], Chiu-Ritchie-Rogart-Stagg-Sweeney model [10], Schwarz-Eikhof model [11].

In this work we use Fitzghugh-Nagumo model that reduces HH model to 2 equations. Despite gross simplification incorporated in this model, simulation is able to qualitatively reproduce behavior of actual biological excitable membranes.

The FitzHugh-Nagumo neuron model in presence of inhomogenously applied HF stimulation current is described as

$$\frac{\partial v}{\partial t} = v - \frac{v^3}{3} - w + D\frac{\partial^2 v}{\partial x^2} + a(x,t)\cos(\omega t) \tag{1}$$

$$\frac{\partial w}{\partial t} = \varepsilon(v + \beta - \gamma w) \tag{2}$$

Equation (1) describes the dynamics of the membrane potential v, where D is the diffusion coefficient and parameters a and ω define the amplitude and frequency of HF stimulation current induced by electrode. Equation (2) defines the dynamics of the slow recovery variable w with a positive rate parameter $\varepsilon \ll 1$. The parameters β and γ are chosen such that without HF stimulation ($a = 0$) the neuron is in an excitable regime. In numerical simulations presented below, we take $D = 1$ without loss of generality [4].

3 Simulation of the model in Matlab

Fitzhugh-Nagumo model represents system of 2 nonlinear PDE in one space dimension that can be solved by Matlab function `pdepe`, (no special toolbox for PDE solution is required).

Let us consider system of nonlinear partial differential equations in one space dimension. In this case, the predefined function `pdepe` allows us to solve initial boundary value problems for system of parabolic-elliptic PDEs in 1D. The class of parabolic-elliptic PDEs, defined in $a \le x \le b, t_0 \le t \le t_f$, to which the function can be applied, has the form [12]:

$$\mathbf{C}(x,t,\boldsymbol{u},\boldsymbol{u}_x)\boldsymbol{u}_t = x^{-m}\partial_x\left(x^m \boldsymbol{f}(x,t,\boldsymbol{u},\boldsymbol{u}_x)\right) + \boldsymbol{s}(x,t,\boldsymbol{u},\boldsymbol{u}_x) \tag{3}$$

where $\boldsymbol{u}$ is a vector-valued unknown function that depends on a scalar space variable x and a scalar time variable t; the flux function $\boldsymbol{f}$ and the source function $\boldsymbol{s}$ are vector-valued functions; the integer $m \in \{0, 1, 2\}$ corresponds to slab, cylindrical, and spherical symmetry, respectively; the function $\mathbf{C}$ is a diagonal matrix whose diagonal entries are zero or positive (which corresponds to elliptic or parabolic equations, respectively). Initial condition at $t = t_0$ and for $a \le x \le b$ and a given function $\boldsymbol{u}_0$ is defined as follows:

$$\boldsymbol{u}(x,t_0) = \boldsymbol{u}_0(x) \tag{4}$$

The boundary conditions at $x = a$ and $x = b$ and for $t_0 \le t \le t_f$ have the form:

$$\boldsymbol{p}(b,t,\boldsymbol{u}) + \boldsymbol{q}(b,t)\boldsymbol{f}(b,t,\boldsymbol{u},\boldsymbol{u}_x) = \mathbf{0} \tag{5}$$

where $\boldsymbol{p}$ and $\mathbf{q}$ are given vector-valued functions.

Since the predefined function `pdepe` implements a second-order spatial discretization method based on the `xMesh` values, it follows that the choice of `xMesh` is important and can affect the accuracy and cost of the numerical solution (e.g., it is best to define closely spaced `xMesh` points for domains where the solution can vary rapidly with respect to x). The time points in `[t0, tf]` at which the solution is obtained are given in the vector `tSpan`, where `tSpan(1)=t_0`, `tSpan(end)=t_f`, and elements of `tSpan` monotonically increase. Since the time integration in `pdepe` is performed by the stiff ODE solver `ode15s`, the actual time step values are chosen dynamically and do not affect the accuracy and cost.

To apply the `pdepe` function, we denote (v, w) by (u_1, u_2) and rewrite the nonlinear system (1) – (2) as follows:

$$\begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix}\frac{\partial}{\partial t}\begin{pmatrix} u_1 \\ u_2 \end{pmatrix} = \frac{\partial}{\partial x}\begin{pmatrix} u_{1x} \\ 0 \end{pmatrix} + \begin{pmatrix} u_1 - \frac{u_1^3}{3} - u_2 + a(x,t)\cos(\omega t) \\ \varepsilon(u_1 + \beta - \gamma u_2) \end{pmatrix} \tag{6}$$

Function `pdepe` requires to define three functions. These functions provide:

1. description of PDE system,
2. initial condition (IC) specification,
3. boundary condition (BC) specification.

It is convenient to define these functions as nested functions, then model parameter will be visible inside inner functions.

PDE system function returns three arguments: *c* – related to left hand side of PDE system, *f* related to spatial derivative terms, *s* is expressed in terms of state variables and stimulus input (defined in separate function, not listed below).

```
function [c,f,s]=PDEfun(x,t,u,DuDx)
c=[1;1];
f=[DuDx;0];
s=[u(1)-1/3*u(1)^3-u(2)+Stimulus(x,t); e*(u(1)+b-g*u(2))];
end
```

Initial conditions are determined as equilibrium state of the system, obtained by setting all derivatives to zero. These conditions result in cubic equation that is solved using *roots* function

```
v=roots([g/3, 0, 1-g, b]);
v0=v(find(imag(v)==0));
w0=v0-v0^3/3;
```

and initial condition function is

```
function u0=ICfun(x)
u0=[v0;w0];
end
```

Boundary conditions are supposed to be zero.

```
function [pL,qL,pR,qR]=BCfun(xL,uL,xR,uR,t)
pL=[0;0]; qL=[1;1]; pR=[0;0]; qR=[1;1];
end
```

Numerical solution of the model is obtained by calling *pdepe* function from caller (outer) function.

```
sol=pdepe(m,@PDEfun,@ICfun,@BCfun,x,t,options);
u1=sol(:,:,1); u2=sol(:,:,2);
```

4 Results

Outline of the fibre model is depicted in Figure 1: Pathological impulse was elicited by short-duration monopolar impulse stimulus applied at the left end of the fibre and it propagates to the right side. Additionally, high frequency (HF) sinusoidal stimulation is applied approximately in the middle region of fibre. At the right end of fibre we examined, whether a pathological impulse is arrived or not.

Parameters of the model were adopted from [4]: $\varepsilon = 0.008$, $\beta = 0.7$, $\gamma = 0.8$. $D = 1$. Notice that all quantities are scaled (dimensionless). Fiber boundaries are located at coordinates $x_L = -100$, $x_R = 200$. Alternating HF stimulation is modeled as sinusoid of angular frequency 50 (rad), applied between coordinates $x_{sL} = -10$, $x_{sR} = 150$. Pathological impulse is elicited between positions $x_{nL} = -100$ and $x_{nR} = -80$. Amplitude of the sinusoidal stimulus was 30 and for second case it was increased to 60.

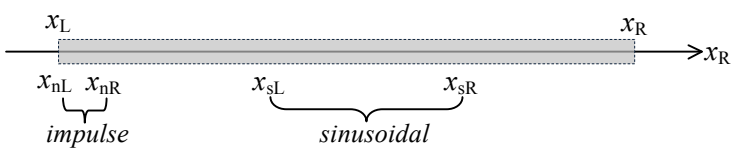

Figure 1: Specification of stimulation regions: region from x_{nL} to x_{nR} for pathological nerve impulse generation and region from x_{sL} to x_{sR} for sinusoidal HF stimulation

Simulation starts at time 0 with sinusoidal HF stimulation. As a response to the onset of the HF stimulation, two action potentials (artefacts) are generated at the end of the stimulated region (x_{sL}, x_{sR}) and propagate in opposite directions (and after time about 150 they are out of observed region of the fibre).

Short-duration monopolar impulse (generating pathological nerve impulse) starts at time 300 and lasts for 50 time units.

In the case of low amplitude (30) of HF stimulation current, pathological impulse propagates across HF stimulated region (Figure 2). As amplitude of HF stimulation increases to 60, propagation of pathological impulse is blocked (Figure 3).

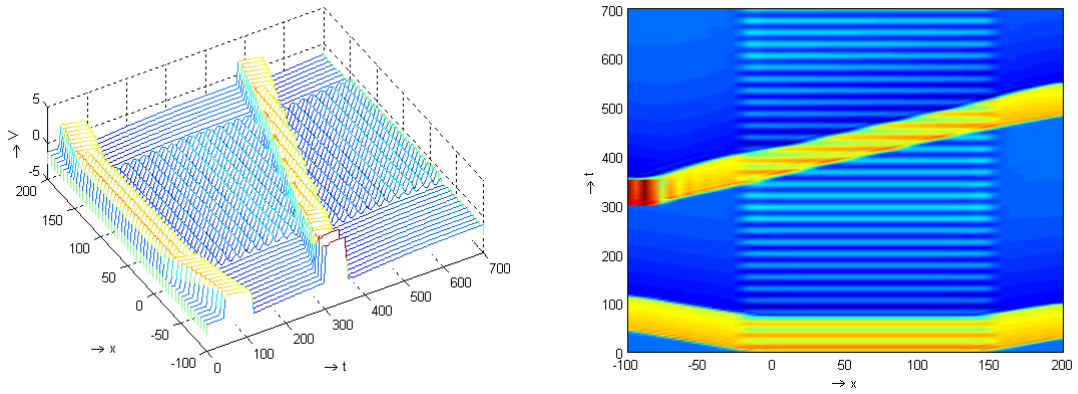

Figure 2: Propagation of neural impulse: low-amplitude of HF stimulation

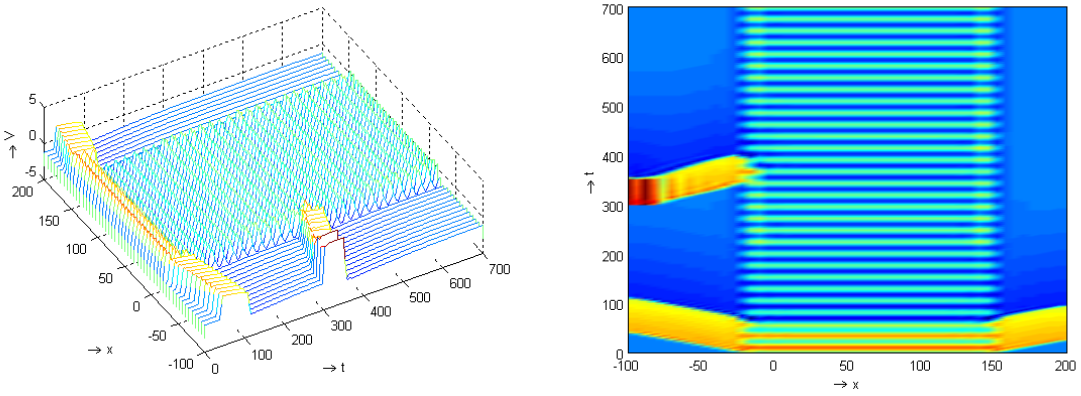

Figure 3: Blockade of pathological neural impulse propagation (high-amplitude of HF stimulation)

5 Conclusion

In this article we outlined possible utilization of Matlab PDE solver in bioengineering, particularly in the neural sciences. Despite simplifications in our model we were able to reproduce

qualitatively the experimentally observed behaviour of nerve fibre for the case of nerve impulse collision with simultaneous high-frequency stimulation signal.

Understanding of the mechanisms of nerve conduction block induced by electrical current is helpful in developing new methods to block pathological impulses propagation along peripheral nerves under different clinical conditions, e.g. in the control of spasticity and pain relieving.

6 Acknowledgement

The research described in the paper was supported under project: Program na podporu mladých výskumníkov:*Elektrostimulácia, monitoring biosignálov a kategorizácia signálov u detí s DMO*.

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