THE USE OF RAMP_SHAPED STIMULUS WAVEFORM FOR SELECTIVE STIMULATION OF NEURAL FIBERS IN PERIPHERAL NERVES

A. Mahnam*, S.M.P. Firoozabadi**, S.M. Hashemi*, M. Janahmadi***

* Faculty of Biomedical Engineering, Amirkabir University of Tech., Tehran, IRAN
** Department of Medical Physics, Tarbiat Modares University, Tehran, IRAN
*** Department of Physiology, Shaheed Beheshti University of Medical Sciences, Tehran, IRAN

amahnam@aut.ac.ir

Abstract: Simulation studies have shown that ramp-shaped under-threshold depolarizing prepulses can invert the current distance relationship and thus be used for selective stimulation of distant fibers from the electrode in a homogeneous medium [1]. In this study, an anisotropic, inhomogeneous model of peripheral nerve trunk in addition to a nonlinear model of neural fibers was used to assess the applicability of this selective technique with multi contact cuff electrodes for real applications. It is shown that this technique can be used to selectively stimulate some central neural fibers of the nerve without activation of lateral fibers.

Introduction

In Functional Neuromuscular Stimulation technique, peripheral nerves are stimulated to restore the function of muscles. An ideal neural prosthesis of this type should satisfy three functional criteria. First, it should be able to activate different muscles or muscle groups of desire, independently. Second, the stimulation should allow for smooth and graded activation of muscles and third, the rate at which the activated muscles fatigue, should not exceed the normal rate of muscle fatigue. These criteria are satisfied if the stimulation paradigm could selectively activate different neural fibers in the peripheral nerve [2].

Several approaches have been suggested to improve the selectivity of electrical stimulation of neural fibers in peripheral nerves [3]. Invasive methods using intraneural and epineural electrodes are used for selectively stimulate desired nerve fascicles or neural fibers in a fascicle. But the implantation and stabilization of these electrodes is very hard and the risk of neural damage during and after the implantation is high. In comparison, cuff electrodes are relatively easy to construct and implant and types of them have been shown to be safe for chronic use. Multiple contact cuff electrodes are used to restrict the activated neural fibers to desired regions, but the selectivity provided by these field-shaping methods are limited. It is not possible to stimulate central fascicles of a nerve by this approach. Anode blocking of undesired neural fibers is used for selective stimulation of more distant or narrow fibers in the nerve, but long pulses and relatively high currents are required that may cause neural damage and electrode contact corrosion.

In waveform-based approach, emphasis is on the influence of stimulus waveform and its parameters on nonlinear dynamic system of excitable membrane for improving selectivity of stimulation and inducing special selective capabilities. Special stimulus waveforms have been shown that can change the stimulation pattern of neural fibers in a nerve, based on non-linear properties of excitable membrane and the resulted blocking effect[3][4]. Grill and Mortimer performed some simulation and experimental studies on the effect of prepulses on changing the excitability of neural fibers. They showed that rectangular under-threshold depolarizing prepulses make the selective stimulation of some distant fibers possible by increasing the excitation threshold of nearer fibers [3]. The prepulse changes the state of the membrane to some more unexcitable regions. The prepulse has more influence on near fibers, so increase the threshold of near fibers more than distant ones. This effect changes the threshold-distant relationship slope to negative values for some distances around the electrode.

We studied the adaptability of this method to targeted fibers in different distances from the electrode [1]. We showed that by the use of rectangular prepulses only fibers in a limited region around the electrode can selectively be stimulated. By simulation of the electrical stimulation of neural fibers in homogeneous medium, we studied the extent of fiber positions where they can be selectively stimulated by several prepulse waveforms. We showed that by the use of ramp-shaped prepulses, it is possible to selectively stimulate targeted fibers in a wider range in both distance and diameter domains.

However in real applications, inhomogeneous and anisotropic properties of stimulation medium (volume conductor) may affect the performance of the suggested methods significantly. So the use of ramp-shaped prepulses for selective stimulation should be assessed with more exact models which consider these properties of volume conductor.

In this study, we simulated the stimulation of neural fibers in the inhomogeneous and anisotropic volume conductor of a nerve trunk with a multi-contact cuff electrode around it. We desired to examine the usability

ISSN: 1727-1983 © 2005 IFMBE

of this method to selectively stimulate central neural fibers in the nerve trunk without excitation of lateral ones.

Method

Simulation of electrical stimulation of neural fibers consists of two steps. First for each time step the volume conductor model should be used to evaluate the electrical potential adjacent to each section of the fiber. In this study, a 3D volume conductor model of a nerve trunk was used to obtain distribution of electrical potential along the fibers. A view of this model is shown in Figure 1.

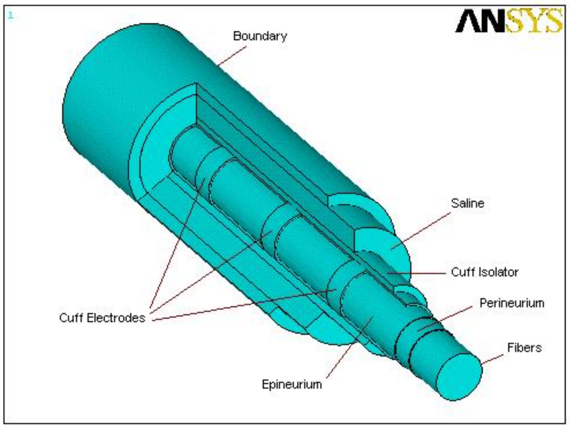

Figure 1: anisotropic and inhomogeneous model of nerve trunk, which a three polar cuff electrode is placed on it.

This model included an anisotropic neural fascicle with the length of 20mm and diameter of 1.9mm covered by perineurium and epineurium layers, each 50um thick. A tri-polar cuff electrode was considered around the nerve. The cuff electrode consisted of three electrode-tips in one row along the fiber with the length of 1mm and thickness of 50um, each covered a 30° Arc of the nerve. An isolator was considered around the electrode tips surrounded by saline. The isolator was 5mm thick and 10mm long. The surrounding saline was considered 0.9mm thick covered by 0.4mm distant medium model. The conductivity of each section was presented in table 1. All the sections were considered purely ohmic. So the volume conductor was linear and without any dynamics.

The model was used for simulation of electrical stimulation with unit current amplitude. The required electrical potentials along the fiber for each time step with the corresponding current amplitudes were calculated based on these results. In this part of simulation, the effect of neural fiber itself was neglected.

To model current injection from electrode tips, the total current was distributed uniformly among the nodes of finite element model on the surface of electrode tips.

The model was implemented by ANSYS software and solved by finite element method.

Table 1: Conductivities of different sections of volume conductor.

Section Name	Conductivity(1/ohm meter)
Nerve Fascicle	0.5 longitudinal, 0.08 radial
Perineurium	0.00336
Epineurium	0.008
Cuff Isolator	0.0008
Saline	2
Distant medium	0.02
Electrode Tip	20

The computed voltage distribution along the simulation time was fed to fiber models as input and the resulted responses of fibers were obtained.

McNeal model was considered for the model of the neural fibers. The myelinated sections of the fiber were considered ideal isolators. Each fiber model consisted of 30 nodes of Ranvier.

Based on this model the current crossing the membrane in each node due to extracellular stimulation is related to membrane potentials and external voltage distribution with this equation:

$$i_{st} = \frac{d\Delta x}{4\rho_i L}\left(\frac{V_{n-1} - 2V_n + V_{n+1}}{\Delta x^2} + \frac{V_{e,n-1} - 2V_{e,n} + V_{e,n+1}}{\Delta x^2}\right) \tag{1}$$

V_n is the variation of membrane potential from its rest value, $V_{e,n}$ is the extracellular voltage adjacent to the node n, d is the axon diameter, D is the fiber diameter, L is the length of the node of Ranvier, Δx is the internodal distance and ρ_i is the intracellular special resistivity. The values of these parameters are presented in table 2.

Table 2: Value of the parameters of fiber model.

Parameter	Value	Unit
ρ_i	55	ohm.cm
L	1.5	um
L/D	100	
d/D	0.6	
Δx	500	um

The nonlinear dynamics of the membrane of each node of Ranvier was simulated by CRRSS model. This model was based on the data from experimental studies on nodes of Ranvier of myelinated axons of rat. The equations of this model are as follows. The parameter values are presented in table 3.

$$\frac{dV}{dt} = \frac{-g_{Na}m^2h(V-E_{Na}) - g_L(V-E_L) + I_{St}}{c} \quad (2)$$

$$\frac{dm}{dt} = k(\alpha_m(1-m) - \beta_m m) \quad (3)$$

$$\frac{dh}{dt} = k(\alpha_h(1-h) - \beta_h h) \quad (4)$$

$$k = Q_{10}^{\frac{T-T_0}{10}} \quad (5)$$

$$\alpha_m = \frac{97 + 0.363V_m}{1+\exp\left(-\frac{V_m - 31}{5.3}\right)} \quad \beta_m = \frac{\alpha_m}{\exp\left(\frac{V_m - 23.8}{4.17}\right)} \quad (6,7)$$

$$\beta_h = \frac{15.6}{1+\exp\left(-\frac{V_m - 24}{10}\right)} \quad \alpha_h = \frac{\beta_h}{\exp\left(\frac{V_m - 5.5}{5}\right)} \quad (8,9)$$

The Model was implemented by Matlab-Simulink software. The simulations were run on a 500MHz Pentium III computer.

Table 3: Parameter values for CRRSS model of excitable membrane.

Parameter	Value	Unit
V_r	-80	MV
C_m	2.5	uF/cm^2
g_{Na}	1445	mS/cm^2
E_{Na}	115	mV
g_L	128	mS/cm^2
E_L	-0.01	mV
m(t=0)	0.003	
h(t=0)	0.75	
T_0	37	°C
Q_{10}	3	

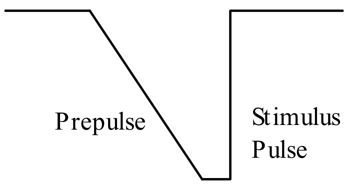

Figure 2: a sample stimulation waveform including ramp-shaped prepulse and stimulus pulse.

Although the modeled cuff electrode was tripolar, bipolar stimulation in the axial direction was used in this experiment. The two lateral electrode tips were used in bipolar stimulation, which were 6mm apart.

Stimulus waveform was consisted of a ramp-shaped depolarizing prepulse followed by a 0.2 mS stimulus pulse. A sample stimulus waveform is shown in figure 2.

The current threshold of different neural fibers in the nerve trunk was calculated for different slopes and widths of ramp prepulse. A transverse view of electrode orientation relative to tested fibers is presented in figure 3.

An action potential was considered that was successfully generated and propagated in a neural fiber, if the membrane potential of its fifth node of Ranvier exceeds zero milivolts.

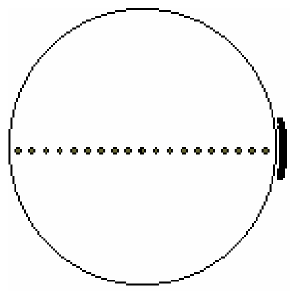

Figure 3: The relative orientation of the electrodes and tested neural fibers in transverse view.

Results

The volume conductor model is used to calculate the voltage distribution due to bipolar electrical stimulation. Figure 4 shows the equi-potential curves resulted from this model.

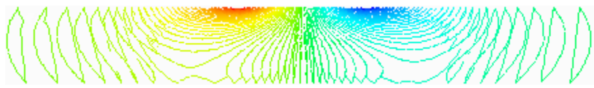

Figure 4: The equi-potential curves produced due to bipolar electrical stimulation.

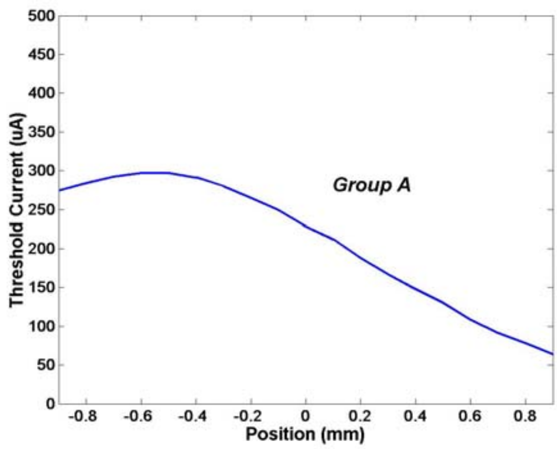

Figure 5: Current threshold for fibers under the study, when rectangular stimulus pulse was used. Electrode was on the right side of the plot. Stimulus pulse width was 0.2mS.

Current threshold was calculated for different fibers along a diameter perpendicular to the electrode (figure 2). Figure 5 shows the result when rectangular pulses are used. Electrode is on right side of the plot. The width of the stimulus pulse was 0.2mS.

As the plot shows, the threshold decreased for lateral fibers at the opposite side of the electrode. The reason is that epineurium and perineurium layers are high in resistivity in comparison to surrounding medium.

Therefore a big portion of the current flows around the nerve under the isolating cuff and forms a non-uniform virtual cuff electrode around the nerve which is of course weak on the opposite side of the real electrode.

The effect of ramp-shaped under-threshold depolarizing prepulse was tested for selective stimulation of some central neural fibers. The results are shown in figure 6 for different prepulse slopes. The width of prepulse was considered 0.4 mS in this study.

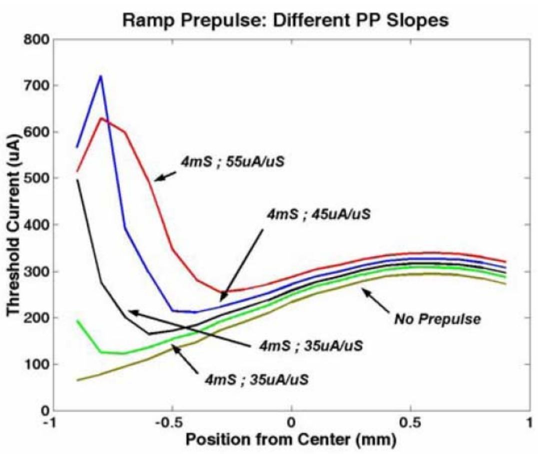

Figure 6: Current threshold of fibers under the study for different prepulse slope, when ramp-shaped under-threshold depolarizing prepulse was used.

As the curves show, the prepulses increased the threshold of near fibers, left somehow central neural fibers excitable by lower current amplitudes. In addition, as the slope of the prepulse increases, the threshold for near fibers also increases. This lets fibers nearer to the center of the nerve be excited selectively. Note that the ramp prepulse increased the current threshold of all the fibers slightly, but this increase is much more for lateral fibers on the side of the electrode. The fibers on the other side were not affected significantly.

Figure 7 shows the current threshold of the fibers, for different prepulse widths. The prepulse slope was considered 55uA/mS.

The increase of prepulse width also increased the threshold for near fibers, but the ratio of threshold increase for near fibers to distant ones is lower in this case. This makes the selective stimulation of central fibers difficult and increase the extent of fibers excited by stimulation.

For high values of slope and width of the prepulse, the threshold for some very near fibers from the electrode is lower that for middle distant ones. The reason is that very near fibers are stimulated by the prepulse itself at lower threshold, while middle distant fibers are still high in threshold under the effect of the prepulse.

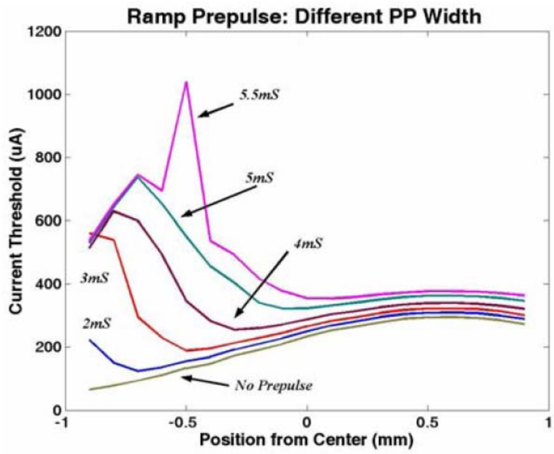

Figure 7: Current threshold of fibers under the study for different prepulse widths, when ramp-shaped underthreshold depolarizing prepulse was used. The prepulse slope was considered 55uA/mS.

Conclusion

By implementing inhomogeneous and anisotropic model of a nerve trunk and nonlinear model of neural fibers, selective stimulation of central fibers of the nerve was tested, using ramp-shaped underthreshold prepulse technique.

The results show that some central fibers can be selectively stimulated by this technique. However the most central fibers of the nerve are still hard to become activated using this method.

By increasing the width and the slope of prepulse more central fibers can be stimulated, but this also increase the extent of the region in which the fibers are excited and decreases the threshold difference between targeted and untargeted distant fibers.

References

[1] MAHNAM A., FIROOZABADI S.M.P. and HASHEMI S.M. (2003): 'Ramp-Shaped vs. Rectangular Under-Threshold Depolarizing Prepulse: Examination of Adaptability to Targeted Fibers', Proc. Of World Congress on Biomed. Eng., 2003.

[2] MUSHAHWAR V. K., HORCH K. W.(2000): 'Selective Activation of Muscle Groups in the Feline Hindlimb Through Electrical Microstimulation of the Ventral Lumbo-Sacral Spinal Cord', *IEEE Trans. Rehab. Eng.*, **8**(1), pp.11-21.

[3] GRILL W.M., MORTIMER J.T.(1997): 'Inversion of Current-Distance Relationship by Transient Depolarization', *IEEE Trans. Biomed. Eng.*, **44**(1), pp.1-9.

[4] GRILL W.M., MORTIMER T.(1995): 'Stimulus Waveforms for Selective Neural Stimulation', *IEEE Eng Med. Biol.*, **14**(4), pp. 375-385.