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Research Article

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Study of the Bioelectricity Effects of Biphasic Pulse Stimulation in the Therapy of Neuromuscular Tissue

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Abstract Relying on the principles of bioelectricity, electrical stimulation assists in the exercise of artificial control over the nervous system. This mechanism propagates action potentials which transmit neural signals to target tissues for diagnostic or therapeutic purposes. Research efforts in electrical stimulation for the activation of compromised neuromuscular tissues have been focused on the control of skin sensation taking into account stimulation parameter such as the nature of the stimulating waveform. This paper is aimed at the simulation study of the bioelectricity effect of biphasic electrical stimulation as applied to achieve nerve activation in muscle tissues with minimal skin sensation. The result of the application of biphasic current stimulating signal to the muscle tissue revealed a slow rise time of the intramuscular voltage inside the muscle which indicated high permittivity of the layers of neuromuscular system under investigation. The implication of this is that the target tissue layers are able to retain electric field sufficiently for activation of nerves without having to increase pulse intensity which can in turn result in painful skin sensation or damage to the nerves.

Keywords Biphasic, electrical stimulation, neuromuscular, therapy, pulses

1. Introduction

Electrical stimulation is essentially the delivery of electrical current pulses using electrodes placed on the skin (transcutaneous delivery) or percutaneously (beneath the skin) in close proximity to the tissue being targeted for rehabilitation. The applied stimulating pulses produce effects similar to the underlying natural bioelectrical response to target tissue. Applications of electrical stimulation include [1]:

i) Facilitation of tissue healing;
ii) Delivery of pharmaceutical substances through the skin to target tissue;
iii) Improvement of compromised neuromuscular functions;
iv) Management and suppression of pain

A nerve cell dedicated to the task of conveying electrochemical pulses throughout the body is known as a neuron. It transmits signals in two directions. Efferent neuron conveys signal from the brain and transmits it to the target tissue while afferent neuron conveys signals from originating tissue to the brain. Neurons are comprised of three sections, namely, a cell body, multiple dendrites and a single axon. The dendrites receive signals while the axon transmits signals to other neurons. The nerve signal is known as action potential. It is generated and transmitted by neurons between the brain and target tissues. The action potential, when generated, is either stimulated, inhibited or modulated [1, 2].

Electrical stimulation assists in the exercise of artificial control over the nervous system based on the principle of bioelectricity. This mechanism propagates action potentials which transmits neural signals to target tissues for diagnostic or therapeutic purposes [2, 19]. Action potential refers to the sudden and transitory change in the potential of excitable membrane such as neurons and muscle cells.

From the diagnostic application perspective, electrical stimulation method has been employed to analyze the function of different regions of the brain. This method is applied to the motor cortex to elicit specific movements of the arm, hand, leg, or face in order to facilitate the understanding of the physiological functions connected to the brain. Additionally, clinical understanding of the condition of impaired speech function has been gained by stimulating nerves in the language areas of the brain.

From the therapeutic application perspective, deep brain stimulation has been applied as a method to provide therapy for conditions of movement disorders. This entails the placement of electrodes in the thalamus, and the effects of the stimulation imitates the effects of a lesion, relieving the tremor and rigidity associated with the condition. The deep brain stimulation has been employed in the treatment of Parkinson's disease, essential tremor, and dystonia as well as other nervous system disorders such as epilepsy, major depressive disorder, and Alzheimer's disease. These therapeutic methods based on electrical stimulation require the placement of electrodes at the target structure and an implantable battery that produces the therapeutic electrical pulses (i.e., internal pulse generator).

Furthermore, the stimulation of large peripheral nerve fibers associated with the spinal cord may be used to suppress activity in the small fibers for the attenuation of pain sensation. Functional electrical stimulation is another therapeutic method that involves the application of electric current pulses either invasively or noninvasively, to nerves and muscles that are paralyzed, usually from spinal cord injury. Some applications of this technique include phrenic nerve stimulation to restore breathing process independent of a ventilator, sacral nerve stimulation to improve bladder and bowel function, and restoration of motor functions in the upper and lower limbs.

1.1 Overview of Biphasic Electrical Stimulation

The efficiency of the result of electrical stimulation can be improved by optimizing size of electrodes and electric field intensity which is a function of current intensity [3, 4]. On the skin surface, electric fields with high strength are typically generated with small electrode size while high skin sensation results from the use of electrodes with large size [5, 19]. Typically, the technique of keeping electrode size constant and varying the current intensity is employed more often than not [6]. However, this method is limited by unwanted skin sensation when intensity value is driven beyond sensation threshold of about 0.4 mA and painful stimulation results at a current value of 3mA [7, 8]. Research attention has been focused on the control of skin sensation taking into account other stimulation parameters. These include composition, geometry, material properties of electrode [5]. Additionally, another crucial parameter consideration for the control of skin sensation is the electrical stimulation waveform. Therefore, this paper is aimed at the application electrical stimulation using biphasic pulse waveform for improved nerve activation with minimal skin sensation.

2. Literature Review

Several studies have been carried out on electrical stimulation of neuromuscular tissues for both diagnostic and therapeutic purposes. Some of the recent studies relevant to this work are summarized in Table 2.1.

Table 2.1: Summary of related works

Author	Stimulation approach	Biphasic pulse features	Stimulation objective	Application area	Conceptual Explanation
Shapiro, et al, [9]	Poststimulation block of nerve conduction	Low frequency biphasic pulses: 1KHz, 500Hz, 100Hz	External urethral sphincter (EUS) contractions	Pudendal nerve conduction block for suppression of pain. Suitable for neuromodulation devices	Generation of large inward sodium and outward potassium currents to produce nerve block due to large changes in axonal intra- and extra-cellular ion

					concentrations that persist after the end of stimulation.
Hsu et al, [3]	Transcranial stimulation	Square and sinusoidal biphasic pulses with frequency >1KHz	Improving intensity level of transcranial electrical stimulation	Reduction of skin sensation	High stimulation intensity causes severe skin sensation in the stimulated areas of the scalp. Low intensity electric field may not be sufficient to produce measurable neural effects.
Shen et al, [10]	electrical stimulation-induced inhibition	charge-balanced biphasic electrical stimulation	Restoration of hearing perception via Cochlear implants based electrical stimulation	Delivery of electrical signals to spiral ganglion neurons	Electrical stimulation can promote the resprouting of spiral ganglion neuron (SGN). This can reduce the gap between cochlear implant electrodes and their targeting SGNs, allowing for an improvement of spatial resolution of electrical stimulation. This in turn can improve hearing perception
Babona-Pilipos, et al, [11]	Electrical stimulation to prevent accumulation of charge and toxic byproducts at lesion sites	Balanced biphasic waveforms	promotion of neural repair in subject suffering from stroke	Enhancement of migratory ability of neural precursor cells with the long-term neural repair	Direct current electric fields promote rapid recruitment and cathode-directed migration of undifferentiated adult neural precursor cells to lesion sites. A phenomenon known as galvanotaxis.
de Oliveira, et al, [12]	Electrical stimulation with randomized inter-pulse intervals, termed nonperiodic stimulation	Biphasic asynchronous stimulation	Enhancement of anticonvulsant effect	Suppression of seizures through desynchronization of epileptiform activity	Epilepsy is a result of neural hyper-synchronization. Electrical stimulation with randomized inter-pulse intervals, termed nonperiodic stimulation (NPS), applied to the amygdala is robustly anticonvulsant.
Arya et al, [13]	Stereo-electro-encephalography	50Hz biphasic	Localization of the seizure-	Language localization	Electrical stimulation mapping (ESM) is

	(EEG) Electrical stimulation mapping	pulses	onset zone		regarded as the clinical standard for localizing language Cortex. Speech or language interference during ESM with stereo-EEG will be a valid classifier of electrode contacts (ECs) lying within language parcels.
Shapiro et al, [14]	Neuromuscular electrical stimulation	35Hz interphase interval to a biphasic pulse	Enhancement of contraction forces of the wrist and finger extensors	Activation of the wrist and finger extensors	Neuromuscular electrical stimulation applied to the muscles that extend the wrist and open the fingers improves joint range of motion and volitional movement, contributing to motor control recovery
Aregueta-Robles, et al, [15]	Subthreshold biphasic stimulation	Balanced charge biphasic pulses	Stabilization of electrode impedance of cochlear implants	Enhancement of sound perception.	Electrodes of cochlear implants undergo impedance fluctuations reportedly caused by protein adsorption and/or inflammatory responses. Hence, the need for impedance stability.
Scheiner et al, [16]	Neuromuscular Electrical stimulation	Imbalanced biphasic signal: dc current density of <35 µA/mm^2	Repair of damaged skeletal muscle tissues	Restoration of motor functions	The electrical activation of the nervous system provides an opportunity to restore missing or impaired body function to systems normally under neural control. This phenomenon is known as neural prostheses.

2.1 Theoretical Formulation

Consider Figure 2.1 which depicts a simple nerve stimulation process that applies a point current source, I_a in close proximity to a uniform myelinated fiber. It is assumed that the current source and the target tissue lie in a uniform conducting medium. Suppose h is the distance between the source and the fiber; d_e and d_i are the diameters of the fiber and the axon respectively and l is the internodal length. In addition, the ratio of internodal length to fiber diameter is assumed to be a constant [20].

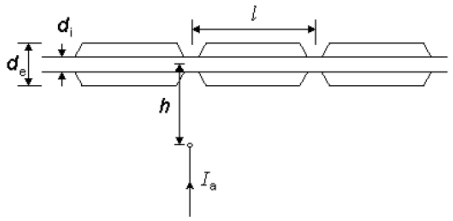

Figure 2.1: A simple point current stimulation a single myelinated nerve fiber [20]

In the Frankenhauser and Huxley (F-H) description of the electric model in Figure 2.1, it is assumed that transmembrane current is confined solely to the nodal region. The membrane model network is basically described by lumped-parameter elements as shown in Figure 2.2 as a parallel RC-structure [20].

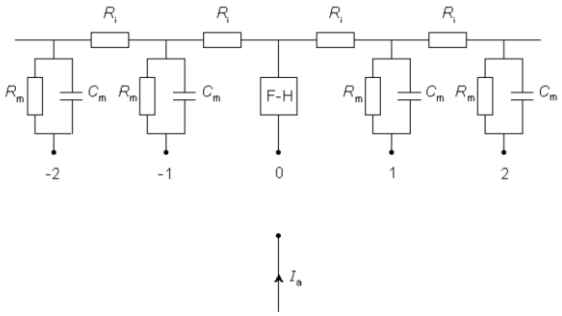

Figure 2.2: Electrical model of a stimulated myelinated fiber

From Figure 2.2, the node directly beneath the applied current source is indexed 0 and its membrane is modeled by Frankenhauser-Huxley (F-H) equations. Adjacent nodes are assumed to be subthreshold and represented by parallel resistance R_m and capacitance C_m (total nodal lumped resistance and capacitance respectively per nodal area). The total intracellular internodal resistance is given by:

$$Internodal\ resistance, r_i = \frac{4\rho_i l}{\pi {d_i}^2} \quad (1)$$

Where:

r_i = axial intracellular resistance per internodal length [kΩ/*l*]

ρ_i = intracellular resistivity [kΩ.cm]

l = internodal length [cm]

d_i = axon diameter (internal myelin diameter) [cm]

The applied stimulating potential field Φ_o is given by:

$$\Phi_o = \frac{I_a}{4\pi\sigma_o r} \quad (2)$$

Where:

Φ_o = Applied potential field [mV]

I_a = Applied current [μA]

σ_o = extracellular conductivity of the medium [kΩ.cm]

r = distance from any node to the point source [cm]

Equation 2 assumes that the extracellular potential from secondary sources within the fiber is negligible and the applied potential field is entirely due to the applied current.

Therefore, the transmembrane current I_m per nodal area at the *n*th node can be determined based on Equation 2 and the network model in Figure 2.2. Let subscripts i and o denote intracellular and extracellular respectively, and *n* the index denoting a specific node (where the central node is indexed 0).

$$I_{m,n} = \frac{1}{r_i}\left(V_{i,n-1} - 2V_{i,n} + V_{i,n+1}\right) = C_m \frac{dV_{m,n}}{dt} + I_{i,n} \quad (3)$$

Where:

$I_{m,n}$ = transmembrane current per nodal area at the *n*th node

$I_{i,n}$ = transmembrane ionic current per nodal area at the *n*th node

$V_{m,n}$ = transmembrane voltage at the *n*th node

C_m = membrane capacitance per nodal area at the *n*th node

r_i = axial intracellular resistance per internodal length

In Equation (3), the intracellular axial current entering the *n*th node is given by the difference expression in the second term of the equation. This difference is equal to the transmembrane current of the *n*th node in which the principle of current conservation is satisfied.

Therefore, the ionic current is given by:

$$I_{i,n} = \frac{V_n}{R_m} \quad (4)$$

where R_m = transmembrane resistance per nodal area (constant).

Since from Equation (3), the transmembrane voltage $V_n = V_{i,n} - V_{o,n}$. Therefore Equation (3) becomes:

$$\frac{dV_{m,n}}{dt} = \frac{1}{C_m}\left[\frac{1}{r_i}\left(V_{m,n-1} - 2V_{m,n} + V_{m,n+1} + V_{o,n-1} - 2V_{o,n} + V_{o,n+1}\right) - \frac{V_{m,n}}{R_m}\right] \; n \neq 0 \quad (5)$$

Substituting Equation (4) in Equation (5) and at $n = 0$, it becomes:

$$\frac{dV_{m,0}}{dt} = \frac{1}{C_m}\left[\frac{1}{r_i}\left(V_{m,-1} - 2V_{m,0} + V_{m,1} + V_{o,-1} - 2V_{o,0} + V_{o,1}\right) - \pi d_i v(i_{Na} + i_K + i_p)\right] \quad (6)$$

where ν is the nodal width, and the ionic currents are found from the Frankenhauser-Huxley equations.

3. Methodology

In this study, layers of the arm tissues were modeled in 2D using COMSOL Multiphysics. The geometry and material properties of the layers were defined as shown in Tables 3.1 and 3.2. In addition, boundary conditions were also defined for the bipolar electrodes used for the biphasic stimulation process. Finally, the intramuscular potential of the stimulation was determined.

Table 3.1: Dimension of model geometric objects [18]

Model Geometry	Dimension
Electrode length	0.03 m
Arm length	0.6 m
Nerve length	0.15 m
Bone marrow thickness	0.013 m
Cortical bone thickness	0.006 m
Muscle thickness	0.0335 m
Fat thickness	0.0025 m
Skin thickness	0.0015 m
Deep nerve depth in Muscle	0.016 m
Surface nerve depth in muscle	0.001 m
Electrode thickness	0.001 m
Electrode gap	0.01 m

Table 3.2: Definition of model material properties [17]

Model Material	Electrical Conductivity [S/m]	Relative Permittivity
Bone Marrow	0.08	10000
Cortical Bone	0.02	3000
Muscle	{0.33333, 0.11111, 0.11111}	{120000, 40000, 40000}
Fat	0.0303	25000
Skin	0.00143	6000
Electrodes	0.00333	1

Biphasic or bidirectional current stimulating signal was applied to the muscle tissue through the skin with pulse duration of 405μs and 2005μs and amplitude of 9 mA was used for the stimulation. The bipolar electrodes arrangement where one electrode serves as conductor for the application of electrical stimulation current pulses and the other serves as the ground terminal to evacuate the charges. The intramuscular voltage was measured

through the two needles inserted into the biceps muscle beneath the skin as shown in Figure 3.1. The quantities of interest are the potentials inside the muscle and at the electrodes. This external measurement showed the stimulation response of the whole system (electrode, skin, fat, muscle) to the applied biphasic current pulse.

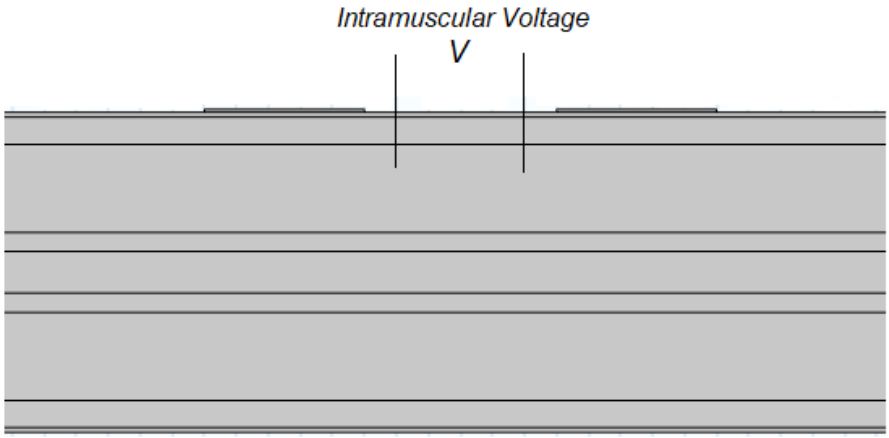

Figure 3.1: Modeled layers of the arm, bipolar electrodes and needles positions for measurement of intramuscular potential

4. Results and Discussion

The two charts in Figures 4.1 and 4.2 show the result of a biphasic current simulation of modeled neuromuscular system for the material parameters in Table 3.1.

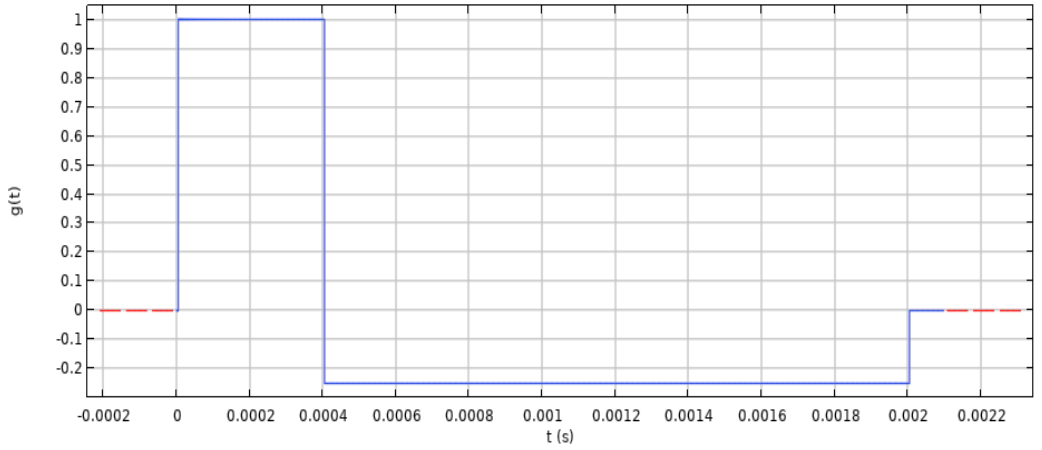

Figure 4.1: Stimulating biphasic current pulse applied at the electrodes

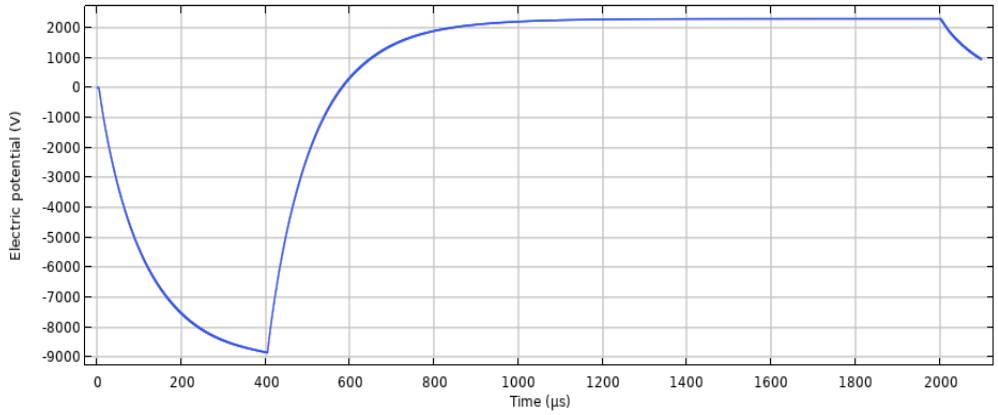

Figure 4.2: Intramuscular voltage in response to stimulating biphasic current pulse

The graph in Figure 4.1 depicts the stimulating biphasic pulse applied at the electrodes which serves as the transcutaneous electrical input. Figure 4.2 depicts the intramuscular voltage response to the electrical stimulation. The simulation results showed that there is a slow rise time of the potential inside the muscle tissue layer defined by the parameters values in Table 3.2. This slow rise time which is about 800μs is due to the high permittivity property of the tissue. This means that the tissue layers are able to sufficiently retain electric field which in effect enables neural activation for a sustained length of time. As a result, the need for increased pulse intensity which can cause painful skin sensation or even nerve damage is avoided.

5. Conclusion

In conclusion, a simulation study of transcutaneous biphasic electrical stimulation for nerve activation was carried out. This was to determine the evolution of the electrical scalar potential inside the human body over time. Biphasic pulse signal was applied to stimulate the muscle tissue with pulse durations of 405μs and 2005μs and amplitude of 9 mA. The electrical stimulation result revealed a slow rise time of the intramuscular voltage inside the simulated neuromuscular system. The slow rise time indicated high permittivity of the material layers of that made up the neuromuscular system. The implication of this is that the target tissue layers are able to retain electric field sufficiently for activation of nerves without having to increase pulse intensity which can in turn result in painful skin sensation or damage to the nerves.

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