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A Simulation Study on the Effect of Phase-shift of Temporal Interference Stimulation

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Abstract

In recent years, stimulation of deep areas by temporal interference (TI) electric fields has attracted much attention. Previous studies have shown the feasibility of stimulating targeted deep areas mouse brain and nerve bundles for stimulation. However, the possibility to change stimulus focus without changing the electrode layout has not been investigated.

In this study, we investigated whether the phase-shift of the TI could be a control parameter for the location of stimulus focus, using a 3D model with 2/3 muscle electrical property.

The potential distribution was measured for different phase-shifting cases. The activating function was calculated and compared to confirm the presence or absence of local focuses.

As a result, it was observed that sites with significant activating function change with a phase shift. Though all the sites appeared near electrodes, i.e., there were no such sites in the deeper part of the model away from the electrodes. This research is a fundamental step towards effective selective deep nerves from the skin surface.

1. Introduction

Recently, Grossman et al. [1] proposed a non-invasive method to selectively activate deep areas using temporal interference (TI) of different high-frequency electric fields. When two electrodes stimulate the object from outside at different frequencies, the interference generates an envelope waveform inside the object. If the generated envelope waveform is large, it may selectively activate the nerves in the deep part of the body. In experiments with mice, hippocampal nerves could be stimulated without affecting the overlying cerebral cortex.

In addition, studies have been conducted to selectively stimulate internal nerves in nerve bundles using this method of temporal interference [2].
However, the possibility to change stimulus focus without changing the electrode layout has not been investigated.
Moreover, there have been no studies on deep nerve stimulation using temporal interference in body regions with a large amount of muscle and fat to the best of our knowledge.

In this study, we investigated whether the phase-shift of the TI could be a control parameter for spatial selectivity, using a 3D model with 2/3 muscle electrical property.

2. Method

To explore the possibility of phase-shift as a parameter to control the location of stimulus focus and confirm whether nerve stimulation surrounded by muscle or fat can be selectively stimulated, we created a finite element simulation model, measured the voltage in the model after applying each stimulus, and derived the activating function.

A 3D cylinder model with a length of 5 mm and a radius of 1 mm using COMSOL Multiphysics® (COMSOL AB/COMSOL, Inc., Sweden) was generated. The size was determined by referring to a related study that showed temporal interference waves might selectively stimulate nerve bundles in the same size region [2].

The inside of the model was set to be a material with the electrical property of 2/3 that of muscle. In this study, the electrical property was set as 2/3 of that of the muscle at a frequency of 100 Hz, the difference between two TI, 100 Hz and 200 Hz (Table I, Table II).

The stimulation waveform was a sinusoidal electrical stimulus oscillating at an effective value of 3mA in positive and negative directions with 0A as the reference. As an initial condition, the electric charge in the model was set to 0C, and the surface of the model was set to have insulating performance so that electrical effects other than the input stimulus were ignored.

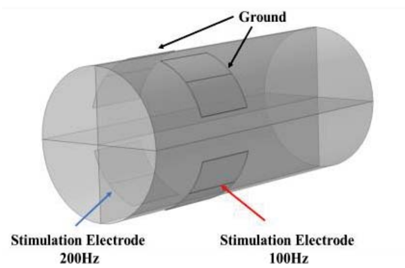

Figure 1. 3D model

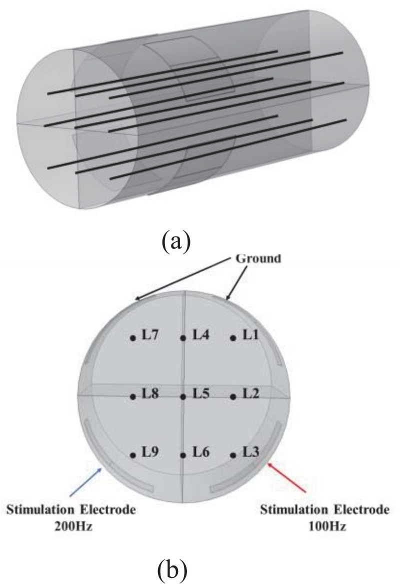

Figure 2. (a) Image of the measurement line (b) Cross-sectional view

Although it is known that the size of the electrodes used should be adjusted depending on the depth of the target nerve [3], in this study, both the ground and stimulating electrodes were set to 2 mm^2 (1 mm × 1 mm) per side. The frequencies of the stimulation input from the stimulating electrodes, 100 Hz and 200 Hz, respectively, were input from the locations shown in Figure 1. Each stimulus was phase-shifted by step by step 60° and measured with a total of 12 different combinations.

The potential distribution of the nine measurement lines "L1~L9" in the model at 250 ms was derived using the above conditions. These lines are used to derive the measurement results of the potential distribution and are not present during the simulation calculation. The nine measurement lines were spaced 0.5 mm apart and were defined along the model's axis (Figure 2).

To evaluate the ease of nerve stimulation from the voltage distribution, we used the Activating function (AF), proposed by F. Rattay [4], to evaluate the ease of nerve stimulation based on the second-order derivative of the spatial distribution of potentials generated at nerve locations by external stimulation.

The magnitude of the activating function at each measurement line was calculated, and the ease of stimulation was examined by comparing the values.

3. Results

The average activating function values on nine measurement lines and in the area directly below the electrodes are shown in Figure 3 when the phase of the 200 Hz stimulation is fixed at 0°, and the phase of the 100 Hz stimulation is varied in steps of 60°. When the 100 Hz stimulation phase is fixed at 0°, and the phase of the 200 Hz stimulation is varied in steps of 60°, the values of average activating function in the area on the nine measurement lines and below the electrodes are shown in Figure 4.

Table I. Conductivity of muscle

Tissue		Conductivity, σ (S/m)
		100 Hz
Muscle	Axial	0.27 [5][6]
	Radial	0.089 [5][6]

Table II. The relative permittivity of muscle

Tissue		Relative permittivity, ε_r
		100 Hz
Muscle	Axial	9.33E+06 [5]
	Radial	9.33E+06 [5]

In both figures, the vertical axis shows the Activating function, and the horizontal axis shows the line number. The average activating function on the line L3, L9 near the stimulating electrode for phase-shifting stimulation waves, changes greatly depending on the phase-shift. The average activating function at L1 and L7 near the ground electrode showed the same change in both phase-shifting of 100 Hz stimulus and 200 Hz stimulus. There was no significant change in the average activating function in other measurement lines as the phase changes.

Figure 5 and 6 show the maximum current density of L1 to L9 for phase-shifted 100Hz, and 200 Hz, respectively.

4. Discussion

The average activation function (Figure 3, 4) and current density (Figure 5, 6) showed different tendencies. For example, L2 and L8 have high current density values, but low activation function. But for L3 and L9, they showed the same tendency. It is reasonable because L3 or L9, which are closer to the stimulation electrodes, are the highest at any phase because the effect of attenuation due to distance on electrical stimulation is the smallest.

In addition, since the value of activating function changed considerably only near the electrode for phase-shifting stimulation wave (ex. L3, L9), it can be considered that the influence of the phase-shift is significant only in a small area near its electrode.

On the other hand, since the activating function at L1 and L7 near the ground electrode varied depending on the phase of 100Hz or 200Hz wave, we consider that the phase variation was a necessary parameter for adjusting the average activating function below the ground electrode. This can be attributed to the effect of the interferential wave generated by the two stimulation waveforms.

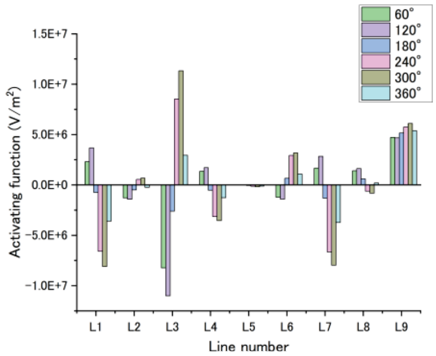

Figure 3. The averaged activation function of each L1-L9 in the under-electrode region for phase shift 100 Hz stimulation.

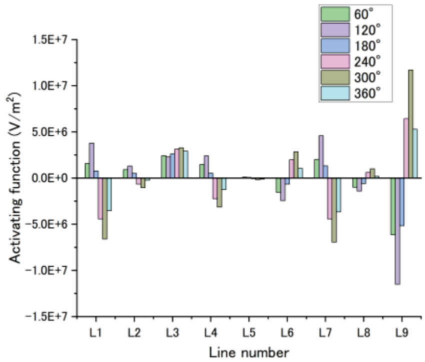

Figure 4. The averaged activation function of each L1-L9 in the under-electrode region for phase shift 200 Hz stimulation.

In other measurement lines, there was no significant change in the average activating function due to the phase change, indicating that it is difficult to selectively stimulate the deep part of the model only by the phase-shift. The reason why the stimulation in the deep part of the model is difficult is thought to be related to the material property filled in the model. In this study, we used a material that has 2/3 of the electrical properties of muscle. Due to the properties of the muscle, the conductivity in the radial direction of the cylinder, which is the expected direction of current flow, is lower than the conductivity in the axial direction of the cylinder, as shown in Table I. We believe that these characteristics may have prevented effective stimulation from reaching the depth of the model and selectively stimulating it.

In the future, we would like to investigate the possibility of deep nerve selective stimulation further using temporal interference on body areas with a lot of muscle and fat by adjusting the input frequency, the current input size, and the model size in addition to the phase change.

5. Conclusion

In this study, we investigated whether temporal interference stimulation, which selectively stimulates nerves surrounded by muscle and fat while changing the phase of the input stimulus, is possible using a three-dimensional simulation model.

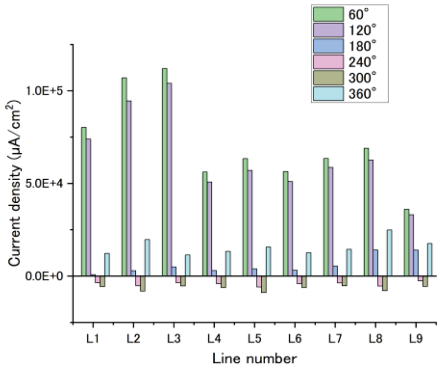

Figure 5. The maximum current density of each L1-L9 during phase shift 100Hz stimulation

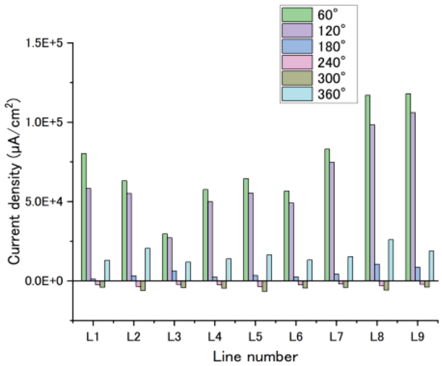

Figure 6. The maximum current density of each L1-L9 during phase shift 200Hz stimulation

As a result, it was difficult to stimulate the nerves in the deep part of the model with the phase-shifted temporal interference waves of 100 Hz and 200 Hz. However, it was suggested that this phase change might contribute to the ease of local stimulation in the area close to the electrode.

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