Modeling Complex Current Waves of a Sural Nerve after Electric Stimulation in case of a Thin Myelin Sheath

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***Abstract*— A nerve conduction test checks whether the function of a nerve to conduct action potentials is normal or not by measuring compound action potential on the skin. In some neuropathies, a decrease in the thickness of the myelin sheath is observed. This is considered to be a cause of any delay or decay of the conduction of compound action potentials. However degenerated nerves include those with missing nerve fibers, which also decreases the velocity and amplitude of the potential. To investigate the effect of myelin sheath exfoliation, the compound action current was defined as modeling the source of compound action potentials, which are constructed as a complex of axonal currents of each nerve fiber inside a nerve. As a result, the thickness of the nerve fiber contributed to slowing the velocity of the current wave; however, the amplitude of the wave did not always decrease.**

I. Introduction

Measurement of skin potential over a peripheral nerve after electric stimulation of the nerve is a common method for diagnosis of any malfunction of peripheral nerves. This method, generally called a nerve conduction test, is both practical and noninvasive. Reductions of amplitude and delay of the conduction velocity of the measured waveform obtained by a nerve conduction test are recognized as typical signs of nerve damage.

The degree of damage to a sural nerve is a possible factor for estimating the condition of various nervous diseases, especially diabetes mellitus, because the distal nerve tends to be affective on metabolic disorder. Also, a biopsy can be performed as it does not include motor nerve fibers. Morphological research has revealed that a decrease in the number of nerve fibers and demyelination are often seen in the nerves of diabetic patients [1]–[5]. However, it is quite difficult to estimate the amount of nerve fibers that have disappeared or the extent of the damage to myelin sheaths. To find the relationship between the condition of a damaged nerve and the measured potential, computer simulation seems an efficient methodology.

As the sources of the potential are the axonal currents of each fiber inside the nerve, it appears important to consider and compare the distribution of the axonal current of normal nerves and injured ones . Therefore, in this paper, we introduce an electric current model of an active nerve after electric stimulation to ascertain electric features of degenerated sural nerves.

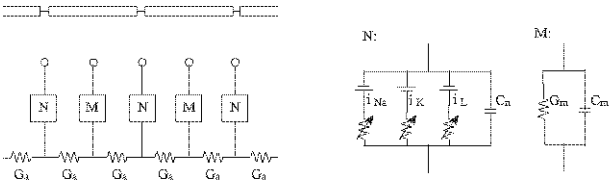

Fig. 1. Nerve fiber model used as components of a nerve. G_a: Axoplasm conductance; i_{Na}, i_K, i_L: Nodal currents of potassium, sodium, and leakage; C_n: Nodal capacitance; G_m, C_m: Myelin conductance and capacitance.

II. Methods

A. Fiber model

Each fiber was modeled as a cable of a Ranvier's node and a myelin sheath. The interval of the node, the axon diameter, and other parameters to define the characteristics of the ion dynamics of the membrane were also modeled in accord with experimental data of human sural nerves [6]. A myelin sheath was modeled as a reel of lamellae; electrically considered as a parallel circuit of a resister and a capacitor [7](Fig. 1). The relationship between the diameter of the axon and the thickness of the myelin sheath in the case of healthy nerves followed previous findings [8]. The number of lamellae n_l was determined as a function of the nerve fiber diameter using the following equation:

$$n_l = 301 \left\{ \frac{(\pi d \cdot 10^6)^2}{4} \right\} + 10. \quad (1)$$

B. Maximum excitable distance

When a nerve fiber immersed in a homogeneous conductor is stimulated with a monopolar electrode, if the same stimulation current I_s is given from the electrode, the threshold distance l_e to make the fiber excitable may be found as follows.

The stimulation of nerve fibers can be drawn as Fig. 2. Where G_e denotes the conductance generated by the external medium causing the current flow between the electrode and Ranvier's node or the myelin sheath. G_e may be described as:

$$G_e(n) = \frac{1}{4\pi r(n)\rho_e} \quad (2)$$

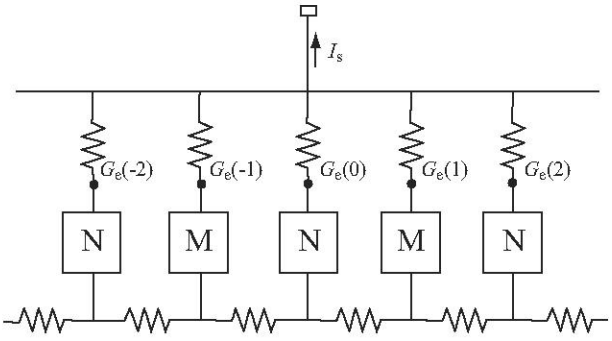

Fig. 2. An equivalent circuit of a nerve fiber under stimulation.

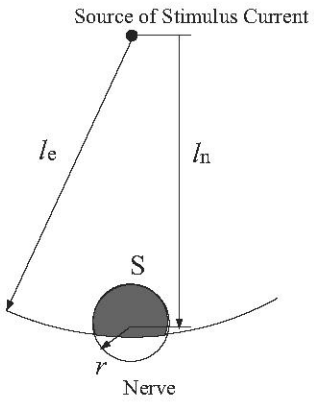

Fig. 3. The principle for the approximation of the sum of the axonal currents of nerve fibers inside a nerve.

where $r(n)$ is the distance between the electrode and the n the node or sheath, ρ_e denotes the conductivity of the external medium. A rectangle pulse wave of 100 mA amplitude and 100 μsec duration was used for the stimulation model. The excitation of a nerve fiber was determined as the increase of the electric potential of the Ranvier's node nearest to the stimulating electrode after 100 μsec from the stimulation ceasing. The maximum excitable value for l was found to be l_e for a fiber of a particular diameter. The value of l_e was calculated for every morphologically different nerve fiber.

C. Total axonal current

Nerve fibers with a specific diameter inside a nerve were assumed to have uniform distribution in a cross section. For n threads of nerve fibers of diameter D, the sum of the axonal current at the position x can be described as $i_D(x)$. If the rate of the number of excitable nerve fibers of diameter D were to be $e(D)$, then the total amount of the axonal currents $I_n(D)$ can be described as:

$$I_{n,D}(x) = n(D)e(D)i_D(x). \tag{3}$$

Here $e(D)$ is the rate of the common area S to the cross section of the nerve and a circle with its center located at the electrode for stimulation, having a radius l_e, to the area of the cross section of the nerve (Fig.3). It can be described as:

$$e = \frac{S}{\pi r^2} \tag{4}$$

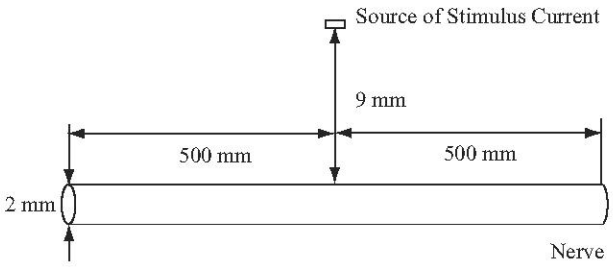

Fig. 4. Nerve and electrode location for the simulation.

where r denotes the radius of the nerve. Therefore, the total axonal current l_n would be expressed as:

$$I_n(x) = \int n(D)e(D)i_D(x)dD. \tag{5}$$

To remove the digital image artifacts contained in the current wave obtained with this equation, A moving average of 20 mm width was applied four times.

III. Condition of the Simulation

A. Nerve model

The nerve model was assumed to be a straight, cylindrical tube 1 m long and 2 mm diameter (Fig. 4). It was constructed as a bundle of myelinated nerve fibers with diameters ranging from 1 to 14 mm. The number of fibers of each diameter was as in an earlier anatomical study of human sural nerves [9]. The thickness of the myelin sheath of the nerve fibers inside a nerve was assumed as in the three cases below.

1. The number of lamellae n_l is normal, as obtained by equation (1).
2. The number of lamellae is reduced to 50% of the normal value.
3. The number of lamellae is reduced to 20% of the normal value.

The number of myelinated nerve fibers inside the nerve was assumed as 190.

B. Stimulation model

A rectangle current pulse of 100 msec duration was given at a point 10 mm away from the core of the nerve over the midpoint from both edges. A semi-infinite homogeneous conductor was assumed between each fiber and the point of the current injection. Mutual electrical interaction between fibers was neglected.

IV. Result

Fig. 6 shows the calculated current wave at 5 msec after stimulation. The waveform varied according to the change of the distribution of the number of nerve fibers and the thickness of the myelin sheath. The decrease in thick fibers slowed the velocity of the total distribution of the axon current. However, in case of (b), in spite of the loss of thick fibers compared to (a), an increase was observed for the amplitude of the positive peak of the wave. Similarly in the case of (g), in

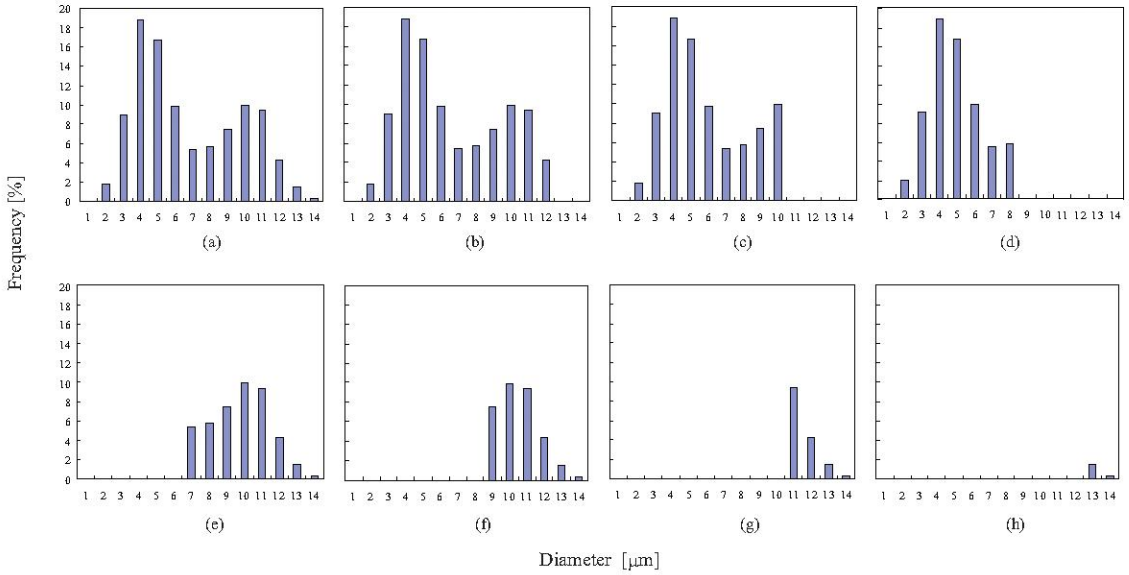

Fig. 5. Distributions of the fiber diameters assumed in this paper.

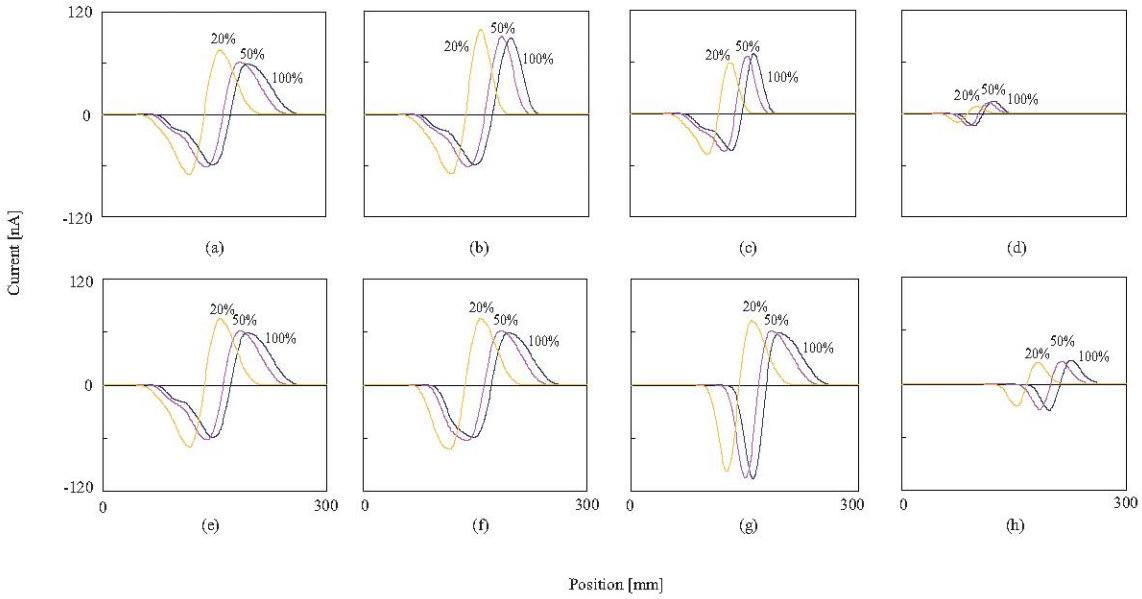

Fig. 6. Simulated current of a sural nerve 5 msec after stimulation.

spite of the loss of thin fibers compared to (e), an increase was observed for the amplitude of the negative peak of the wave. The decrease of the myelin sheath slowed the conduction velocity in many cases of the diameter distributions; however, the amplitude increased in some cases but decreased in others. Fig. 7 shows the conduction velocities of each fiber diameter distribution. For the normal fiber diameter distribution (a), the conduction velocity of the positive peak was always faster than the velocity of the negative one; however, in some cases with lost fibers, the velocities of both peaks almost corresponded. Fig. 8 shows the decay process for the amplitude of the positive peak of the current wave. In the case of enough thick fibers remaining inside the nerve ((a), (b), (e), (f)) the amplitude decreased rapidly with the passage of time. However, in the other cases the decrease was milder or no decrease was observed. In the case of a thinner myelin sheath, the decrease slowed; however, the difference was small compared to the effect of the fiber diameter distribution.

V. Discussion

The conduction velocity of the current wave became slower in accord with the reduction of the thickness of the myelin sheath in each of the cases of nerve fiber diameter distribution. This is consistent with the accepted view that conduction

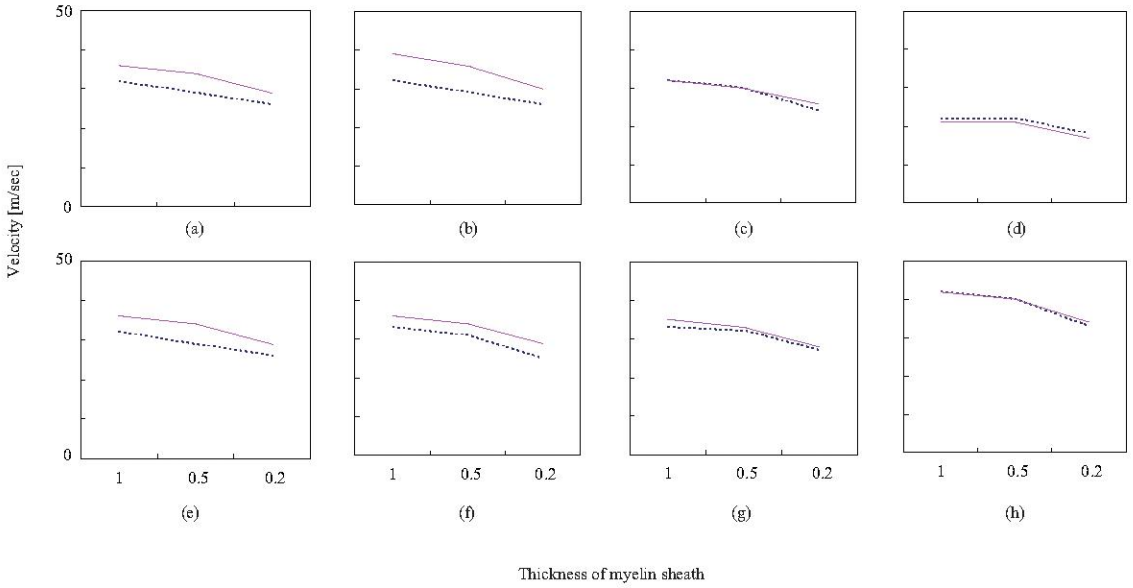

Fig. 7. Conduction velocity of the current wave. Solid line: positive peak; Dotted line: negative peak.

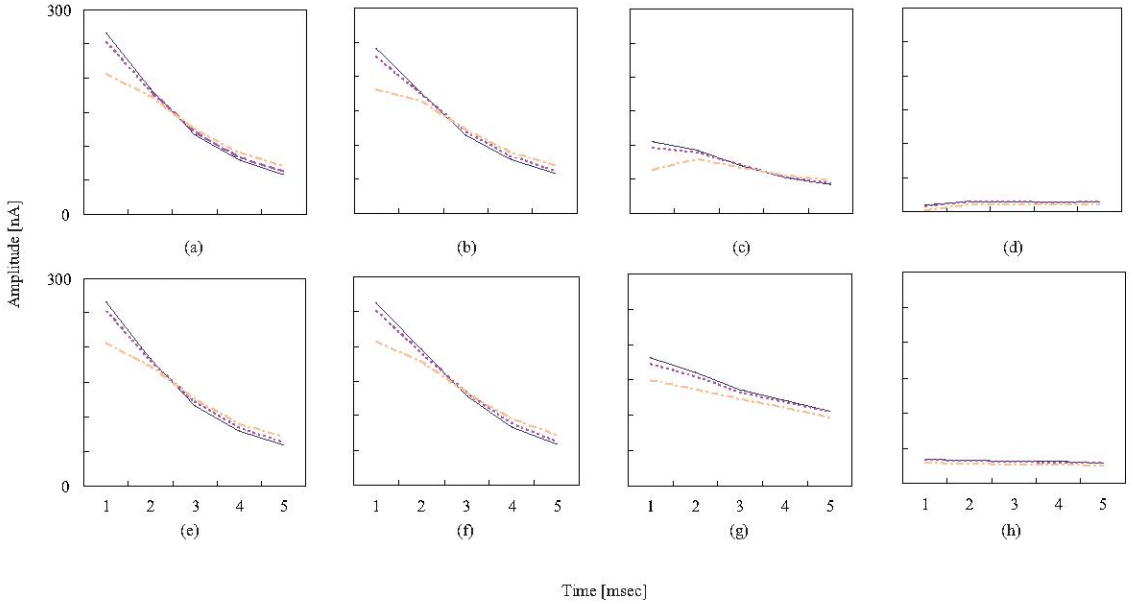

Fig. 8. Amplitude of the positive peak of the current wave. Solid line: the thickness of myelin sheath is normal. Dotted line: the thickness of myelin sheath is 50% of the normal value. Dash-dotted line: the thickness of myelin sheath is 20% of the normal value.

velocity decreases in demyelinating neuropathy. However, the amount of the decrease in the conduction velocity was logarithmic to the decrease of the thickness of the myelin sheath, which caused just a few percent points of the reduction of the conduction velocity, despite there being fifty percent exfoliation of the myelin sheath. In respect to diabetic neuropathy, as a degenerated nerve includes both missing nerve fibers and demyelinated ones, it may be difficult to estimate the grade or type of demyelination from the current distribution because the change of the diameter distribution had more effect on the shape of the current wave than the changes to the myelin sheath.

In plots (a)(b)(e)(f) in Fig. 6, the conduction velocity of the positive peak is always faster than that of the negative one, although in the other cases, the velocities of each of the peaks were consistent. The difference in the velocity between positive and negative peaks seems to be affected by the distribution of nerve fiber diameters, but seem hardly affected by the thickness of the myelin sheath.

The attenuation rate of the amplitude of the positive peak was also higher for the diameter distributions in (a)(b)(e)(f) than the other cases (Fig. 8). This also reflects the distribution

of nerve fiber diameters. The exciting threshold of a nerve fiber rises as the myelin sheath becomes thinner, which causes the inactivation of thin fibers and decreases the current wave amplitude. However this effect seems to have disappeared around 2 msec after the stimulation as the current distribution is diffused because each fiber has a different conduction velocity.

VI. Conclusion

A total axonal current model was introduced to express the electric signal conduction of a peripheral nerve after electric stimulation. We simulated the stimulation of a damaged sural nerve with nerve fiber loss and myelin sheath exfoliation. Our analysis of the simulated current wave showed that although fibers with a thin myelin sheath decrease the conduction velocity, they do not always decrease the amplitude of the wave.

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