Detection of Nerve Action Potentials Under Low Signal-To-Noise Ratio Condition

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***Abstract*—We propose a method for detection of action potentials (APs) under low signal-to-noise ratio condition. It is based on multiresolution analysis. Three parameters are used for detection. Two of them are for determining if there is an AP or not, and the other is for the estimation of waveforms. Our method provides better estimated waveforms than the conventional de-noising approach.**

***Index Terms*—Cuff electrode, low signal-to-noise ratio condition, multiresolution analysis, nerve action potentials, wavelet transform.**

I. Introduction

Sensory and motor command information is considered to be represented by neural activity patterns. Recordings of neural activity provide us a clue to estimate this kind of information from peripheral nerves. Therefore, neural recordings are of significant importance to applications in both scientific and clinical areas.

There are several types of recording electrodes. Cuff electrodes [1] can be used for long-term recording [2] because they cause less damage to the nerve fibers than intrafacicular electrodes such as wire electrodes, regeneration microelectrode arrays [3], [4] and slanted multielectrode arrays [5]. However, it is sometimes difficult to detect action potentials (APs) from cuff recordings by conventional amplitude detection scheme because the signal-to-noise ratio (SNR) of cuff recordings is smaller than that of intrafacicular recordings.

In order to compensate for the shortcoming of the cuff electrode, we developed a method for detection of APs under low SNR condition. If the noise process contributes the same frequency bands as the signal, conventional filtering approach faces serious difficulties [6]. De-noising approach [7], [8], which is the noise removing scheme based on multiresolution analysis (MRA), with proper threshold can suppress white noise process by damping or thresholding wavelet coefficients. In this paper, we focused on a new thresholding rule to obtain a better estimation of the waveforms of APs than the conventional de-noising approach. Our method uses three parameters, whereas the conventional de-noising approach uses only one. Two of them are for determining if there is an AP or not, and the other is for the estimation of waveforms.

We evaluated the performance of our method with both a simulated signal generated by a peripheral nerve model and a real signal recorded with a cuff electrode.

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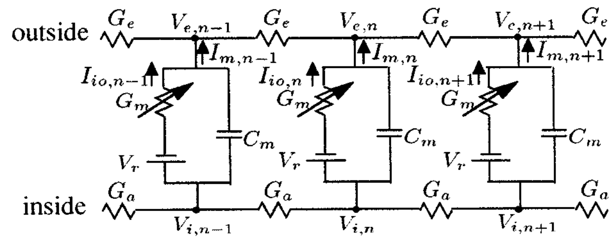

Fig. 1. Electrical circuit representation of a myelinated nerve fiber. The membrane capacitance C_m, the resting potential V_r, and the nonlinear membrane conductance G_m represent the gating of the ionic channels and decide the value of the ionic current $I_{io,n}$ at node n. $V_{i,n}$ and $V_{e,n}$ are the internal and the external potentials, G_a and G_e are the axoplasmic and the extracellular conductance, and $I_{m,n}$ is the membrane current at node n.

II. Methods

A. Simulated Signal

The simulated signal has some advantages over the real neural signal for evaluating the performance of the algorithm, because it provides known solutions with different conditions, like firing time and various SNRs.

The simulated signal was generated by a peripheral nerve model. The assumptions for developing the model generally follow those of McNeal [9], except that we assumed there is variation in potential over the nodal surface. The nerve fiber was expressed by an electrical circuit (Fig. 1). Frankenhaeuser–Huxley equations [10] specified the membrane capacitance C_m, the resting potential V_r, and the nonlinear membrane conductance G_m which represent the gating of the ionic channels and decide the value of the ionic current $I_{io,n}$ at node n. When the membrane at the end of the fiber is depolarized, an AP is generated and it is conducted along the fiber following the first-order differential equation:

$$C_m \frac{dV_{m,n}}{dt} = \frac{G_a G_e}{G_a + G_e} (V_{m,n-1} - 2V_{m,n} + V_{m,n+1}) - I_{io,n}$$

where $V_{m,n}(=V_{i,n} - 2V_{e,n} - V_r)$ is the transmembrane voltage at node n, and G_a and G_e are the axoplasmic and extracellular conductance/unit length of axon, respectively. The nerve trunk was assumed to be an infinite homogeneous volume conductor

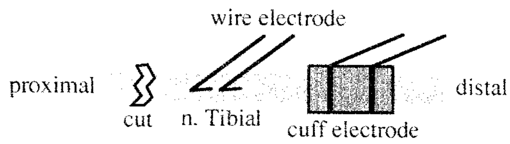

Fig. 2. The arrangement of recording electrodes. A neural signal related to the angle changes of the MTP were recorded from both inside and outside of the tibial nerve with the cuff and the wire electrodes, respectively. The nerve was cut at the proximal side in order to block spinal reflexes.

for calculating the surface potential of the nerve trunk, and the neural signal was obtained by bipolar recording. The frequency components of generated neural signal were limited to between 100 Hz and 2 kHz with a bandpass filter.

A Gaussian noise process was generated by the minimal standard generator and the Box–Muller method [11], and the frequency components were limited with low-pass filter whose cutoff frequency was 4 kHz. The simulated signal was obtained by adding a Gaussian noise process to the neural signal.

B. Cuff Electrode and Recording Methods

We used 75-μm stainless-steel wire with Teflon coating (SUS316, A-M systems) as a recording electrode, because the excess noise generated from stainless-steel was smaller than from other metals [12]. Teflon coating was removed from the wire at the tip of it for recording, and it was sewn on the cuff, which was made from silicone tube. Internal diameter of the cuff was 2 mm and length was 8 mm. The cuff electrode was designed for bipolar recording. The distance between recording electrodes was 5 mm. The peak-to-peak amplitude of the noise process generated from the recording electrode was about 3 μV_{pp} when the frequency components were limited by an analog bandpass filter with cutoff frequencies at 15 and 3 kHz.

As shown in Fig. 2, the cuff electrode was placed on the tibial nerve of a Japanese white rabbit which was anesthetized by pentobarbital sodium. Wire electrodes were inserted into the nerve at the proximal side of the cuff electrode to record the neural signal simultaneously. The distance between the cuff electrode and the wire electrode was about 10 mm. In order to block spinal reflexes, the nerve was cut at the proximal side of the wire electrodes. The neural activities related to the angle changes of the metatarsophalangeal (MTP) joint of the forefinger were recorded. Neural signals were amplified with a differential amplifier (MEG-2100, Nihon Koden) with a gain of 80–100 dB, filtered by an analog bandpass filter with cutoff frequencies at 15 and 3 kHz and recorded with a tape recorder (RD-135T, TEAC). After the experiment, recorded signals were sampled at 20 kHz and analyzed with a personal computer (Power Macintosh 7600/132, Apple Computer Inc.).

C. Estimation of Statistical Characteristic of the Noise Process

With the amplitude histogram of the recorded signal, we estimated the mean and the standard deviation (SD) of the noise process in the presence of the neural activity. The estimated statistical characteristic was used to decide the value of parameters for detection of APs.

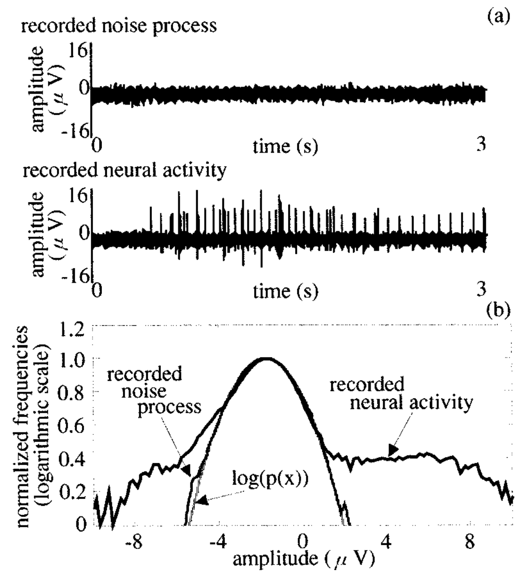

Fig. 3. The recorded time series and their amplitude histogram. (a) The neural activity related to the angle changes of MTP were recorded with wire electrode. (b) The amplitude histograms of the recorded noise process and the recorded neural activity, and $y = \log(p(x))$ are plotted. Where $p(x)$ is the probability density function of the normal distribution.

The amplitude distribution of the Gaussian noise process follows the normal distribution and the probability density function $p(x)$ is defined as

$$p(x) = \alpha \cdot \exp\left\{-\frac{(x-\mu)^2}{2\sigma^2}\right\} \qquad (\sigma > 0, \mu \in \mathrm{R}) \qquad (1)$$

where

μ mean;

σ SD, respectively;

α constant.

Although the amplitude distribution of the recorded signal does not follow the normal distribution in the presence of neural activities, the main contributions to classes which have large frequencies are not neural activities but the noise process and the amplitude distribution of those classes almost follows the normal distribution as shown in Fig. 3. The number of classes C of the histogram was decided by the following equations:

$$C = 1 + \log_2 m \qquad (2)$$

where m is the number of sampling data. We estimated the statistical characteristic by means of fitting (1) to the distribution of the classes whose frequencies are greater than two-thirds of maximum frequency with the least square method.

D. Detection of Nerve Action Potentials

The hierarchical structure of the MRA generated by wavelets (Fig. 4) was used for the detection of APs. Although the orthogonal wavelets of Daubechies have been dominantly used in most of the wavelet analyses, their values may not be computed in a straightforward way. On the other hand, the compactly supported cardinal B-spline wavelets constructed by Chui and Wang [13], which are biorthogonal functions, have several desirable properties in applications. Some of them are as follows [14].

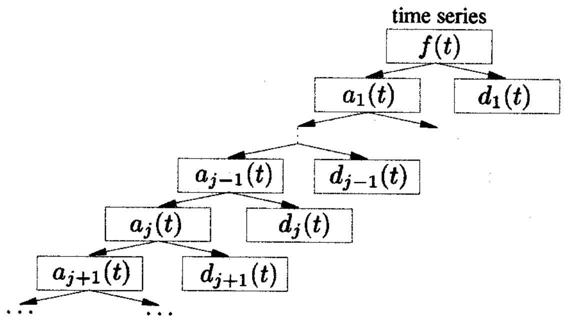

Fig. 4. The hierarchical structure of the MRA generated by wavelets. $f(t)$ is time series data, $a_j(t)$ is discrete approximation of $f(t)$, and $d_j(t)$ is discrete detail signal at scale j.

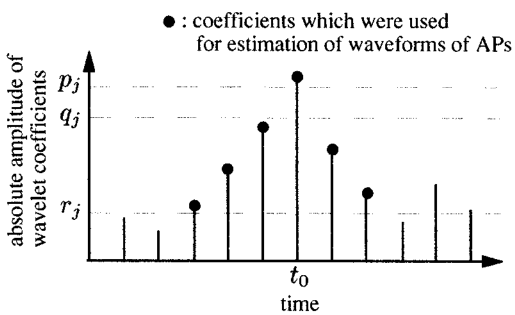

Fig. 5. Our method uses three thresholds for detection of APs. The higher threshold p_j determines if there is an AP or not. q_j is used as a threshold to confirm the presence of an AP, if an AP has been probably detected at a continuous scale. Once the presence of an AP is confirmed, we use the lower threshold r_j to estimate the waveform. Wavelet coefficients which are greater than r_j and consecutive with respect to time t_0 are used for the reconstruction of the time series.

- The algorithm can be constructed using only the convolution of discrete data of real numbers and, hence, it is fast.
- Easy interpolation algorithms are available to find the representation of the time series data in terms of the scaling functions.

In this paper, we used the cubic cardinal B-spline [14].

Detection of APs with conventional de-noising approach has three steps [8].

1) Obtain the wavelet coefficients (discrete detail signal) $d_j(t)$ at scale (frequency band) j of the recorded signal.
2) Apply the hard-thresholding to each scale

$$\eta(d_j(t)) = \begin{cases} d_n(t): & |d_j(t)| > th_j \\ 0: & |d_j(t)| \le th_j \end{cases}$$

where
$th_j \quad = \sigma_j \sqrt{2 \log_e m_j}$;
m_j number of sampling data;
σ_j SD of the noise process at scale j.

3) Reconstruct time series with the threshold wavelet coefficients $\eta(d_j(t))$.

In conventional de-noising approach, if the threshold th_j is set to be large, the number of false positive decreases. However, more and more components of waveforms of APs are zeroed out and the distortion of the waveforms becomes large. Therefore, we used three parameters. As shown in Fig. 5, two of them are for determining if there is an AP or not, and the other is for the estimation of waveforms.

A threshold amplitude p_j at scale j, to determine if there is an AP or not, was defined as

$$p_j = z(x_j) \cdot \sigma_j \tag{3}$$

and if the wavelet coefficients at scale j of the time series at time t_0, $d_j(t_0)$, satisfied

$$|d_j(t_0)| > p_j \tag{4}$$

we supposed that it is possible that there is an AP at time t_0. x_j is the probability and $z(x_j)$ is significance level of the normal distribution for the null hypothesis that there are no APs, σ_j is the SD of the noise process at scale j. The number of false positives was limited to be less than 1/20 s, namely x_j satisfied

$$(1 - x_j)n_j = 0.05 \tag{5}$$

where n_j is the number of sampling data/s at scale j.

We used another threshold amplitude q_j for verifying the presence of AP at time t_0. The value of q_j was $z(0.90)\sigma_j$. In case of an AP, the signal usually appears on two or three continuous scales simultaneously, but in case of the noise process, there is no such correlation. Therefore, if the wavelet coefficients at time t_0 satisfied inequality (6) and/or (7)

$$|d_{j-1}(t_0)| > q_{j-1} \tag{6}$$

$$|d_{j+1}(t_0)| > q_{j+1} \tag{7}$$

we determined that an AP was in the time series at time t_0, and information about waveforms were in the scale j and the next scales which satisfied inequality (6) and/or (7)

A threshold amplitude r_j at scale j to estimate waveforms of APs was used. The value of r_j was $z(0.60)\sigma_j$. The wavelet coefficients for estimation of waveforms of APs were selected from the scales which had information about waveforms of APs. The absolute values of coefficients were greater than r_j and consecutive with respect to time t_0 (Fig. 5). Time series was reconstructed with these coefficients.

III. Results

A. Detection from the Simulated Signal

Our method was evaluated with the simulated signal. Fig. 6 shows the detection ratio against various SNR of the signal. The detection ratio with our method is almost the same as that with the conventional de-noising approach. There was no false positive in both our method and the conventional de-noising approach.

In order to evaluate the distortion of the waveform, we calculated the Euclidean distance between the noise-free and the detected waveforms of APs. Fig. 7 shows the average value of calculated distance of 20 APs. The value is normalized by the distance when the conventional de-noising approach is used. The value of the threshold amplitude r_j for estimation of waveforms was defined as $z(0.60)\sigma_j$ in this paper. We also calculated the Euclidean distance for various values of r_j from $z(0.10)\sigma_j$ to

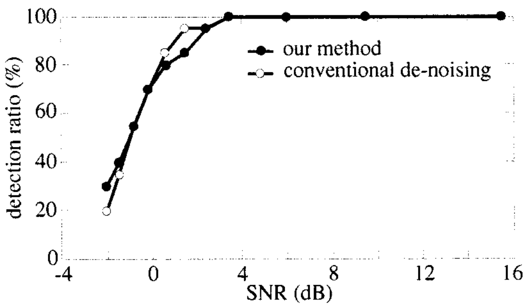

Fig. 6. The detection ratio against various SNR. The frequency components of the neural signal are from 100 Hz to 2 kHz, and those of the noise process are limited with low-pass filter whose cutoff frequency is 4 kHz. The detection ratio of our method is almost same as that of conventional de-noising approach.

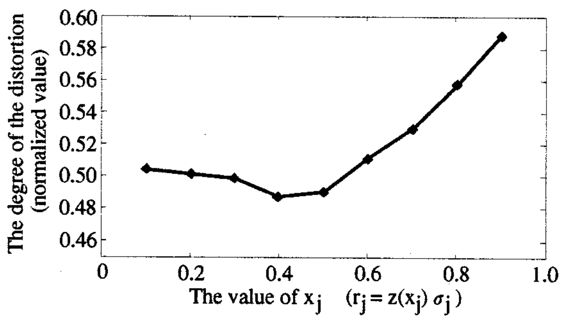

Fig. 7. The distortion of the waveforms of the detected APs. The distortion was evaluated with the Euclidean distance between the noise-free and the detected waveforms of APs. Vertical axis is normalized by the value when the conventional de-noising approach is used. Horizontal axis is the value of x_j which defines the value of the threshold amplitude r_j for estimation of waveforms by $z(x_j)\sigma_j$.

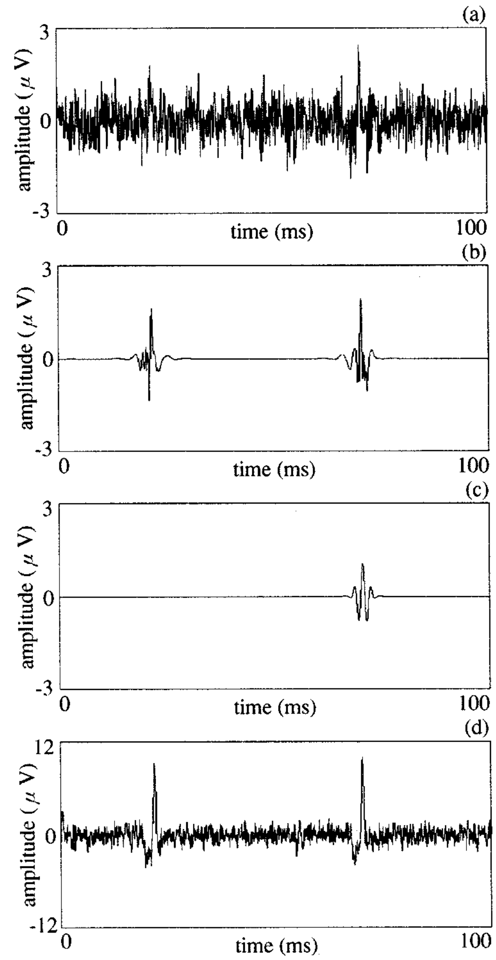

Fig. 8. The recorded neural activity and the detection result. (a) The recorded neural activity, which was related to the angle changes of the MTP joint of forefinger, with the cuff electrode from the tibial nerve. (b) Result of detection from the cuff recordings with our method. (c) Result of detection from the cuff recordings with conventional de-noising approach. (d) The recorded neural activity with the wire electrode which was placed at the proximal side of the cuff electrode.

$z(0.90)\sigma_j$. Fig. 7 shows that our method provides better estimated waveforms than the conventional de-noising approach.

B. Detection from Cuff Recordings

The neural activity was recorded only when the MTP joint was extended. We could record stably while we conducted the experiment. Fig. 8 shows recorded waveforms with both the cuff and the wire electrodes, and detection result. The SNR of cuff recordings is much lower than that of wire recordings. It is difficult to find APs in cuff recordings. Our method detected two APs, although conventional de-noising approach detected one. The firing time of detected APs correspond to those of wire recordings. The detection result by our method is valid if we assume that both the cuff and the wire electrodes recorded the activity of the same units.

IV. Discussion

Our detection method and conventional de-noising approach are based on MRA. The signal is decomposed into a number of scales, the wavelet coefficients, which have information about waveforms of APs, are selected, and the signal is reconstructed with these coefficients. Therefore, advantages of our method and conventional de-noising approach over conventional filtering approach are that they do not need to decide the cutoff frequency for removing the noise process which has different frequency components of the signal, and if the noise process contributes the same frequency bands as the signal, they can suppress this kind of noise process.

Our method uses three parameters for detection of APs, whereas the conventional de-noising approach uses only one. This makes possible to obtain better estimated waveforms than the conventional de-noising approach. The probability of occurring false positive decides the value of parameters p_j and q_j for determining if there is an AP or not. However, there is no criteria to decide the value the parameter r_j for the estimation of waveforms of APs, because the optimal value of r_j depends on the waveforms of the APs and it is difficult to know them under low SNR condition. As shown in Fig. 7, large value of r_j makes the distortion large because the coefficients for reconstruction do not have enough information about the waveforms of APs, and small value of r_j also makes the distortion large because some coefficients have more information about the noise process than about the waveforms of the APs. We assumed that when the value of r_j is between 40% and 60% significance level of the normal distribution for the null hypothesis that there is no APs, r_j is not too large or too small for any kind of waveforms.

Diagnostic device for clinical use requires a real-time system. There were some reports about a digital signal processing (DSP) system to perform wavelet transform in real-time [15]. Applying this kind of DSP systems to our method, our method could be implemented in real-time.

V. Conclusion

In this paper, we have developed the method for detection of APs under low SNR condition. Our method is based on MRA, and uses three parameters. Two of them are for determining if there is an AP or not, and the other is for the estimation of waveforms. Our method provides better estimated waveforms than the conventional de-noising approach.

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