Adaptive Forward-Reverse Filter using Interpolation Methods for Artifact Suppression in Retinal Prostheses

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Abstract: Electrical stimulation on retinal ganglion cells (RGCs) induce the short-latency (directly-evoked) and long-latency (indirectly-evoked) responses of RGCs. The artifact suppression and isolation of direct RGC spike is required for proper analysis of visual information. Adaptive forward-reverse filter (FR filter) using interpolation method is proposed and evaluated. On selected over 1.6 ms waves, which is suspected as artifact, 2 new data points are linearly interpolated between the recorded data points. After that, the interpolated data are filtered by frequency-based FR filter (500 Hz). The proposed algorithm shows the best true positive rate (0.7629) comparing with the SALPA and the simple FR filter without the interpolation method. In point of view of the false positive rate, the proposed algorithm demonstrates the second-best performance (0.0047), not better than the SALPA (0.0006).

1 INTRODUCTION

The outer retinal diseases such as the retinitis pigmentosa (RP) and the age-related macular degeneration (ARMD) are the main causes of most blinding retinal diseases. The retinal prostheses have been regarded as a promising method for restoring vision for the blind with these outer retinal degenerative diseases. Each electrode of retinal prostheses would stimulate remained living-cells in the diseased retina. These stimuli transmit visual information to the visual cortex of the patient brain (Humayun et al., 2003; Jensen and Rizzo, 2008; Ryu et al., 2009b). Retinal prosthesis is classified into two types: epi-retinal prosthesis and sub-retinal prosthesis. Epi-retinal approach for retinal prosthesis stimulates the retinal ganglion cells (RGCs) using the microelectrode array implanted on the retinal surface (Rao et al., 2008). The epi-retinal stimulation can evoke short-latency response and long-latency response. The short-latency response is originated from the direct stimulation of RGCs, and the long-latency response is originated from network mediated stimulation of RGCs (Boinagrov et al., 2014; Sekirnjak et al., 2006). The long-latency responses can be clearly identified without hindrance of the stimulation artifact, however, the short-latency responses are significantly hindered by the stimulation artifact (Jensen and Rizzo III, 2007).

RGCs can accurately follow electrical stimulation with rates up to 250 Hz, which is equivalent to the maximum spike frequencies in the natural light response of the normal eye (Fried et al., 2005). Therefore, direct RGC stimulation may allow precise mimicking of RGC bursts characteristic to normal vision (Sekirnjak et al., 2006). In order to encode visual information properly in the retinal prosthesis, the RGCs responses should be properly isolated (Ryu et al., 2009a; Wagenaar and Potter, 2002).

In the previous researches, several methods have been used to detect the short-latency spike. The typical method is tetrodotoxin (TTX) injection method. The TTX blocks sodium channel so that its injection enables to get spikeless signal, that is, the pure stimulus artifact. The pure stimulus artifact is subtracted from the raw signal containing obscured spikes for the short-latency response detection (Fried et al., 2005; Ryu et al., 2009a; Sekirnjak et al., 2006). Besides the TTX injection method, the patch clamp

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methods and the threshold stimulation method have been researched for the short-latency spike detection (Lee et al., 2007; Li et al., 2005). The above-mentioned methods require additional experimental manipulations to detect the short-latency spikes, such as chemical injection and stimulation strength varying. Furthermore, these methods are almost impossible to apply to the retinal prosthesis system.

In our previous study, we compared results of three different algorithms; suppression of artifacts by local polynomial approximation (SALPA), moving average filter (MAF), and forward-reverse filter (FR filter). These three filter algorithms demonstrated short-latency spike detection feasibility (Choi et al., 2015).

In this paper, we propose the adaptive FR filter using interpolation method for artifact suppression. The FR filter algorithm performs a zero-phase filtering by forward and reverse processing with identical filter (Gustafsson, 1994). In the artifact region, the recorded voltage values are fluctuated dramatically. We interpolate new values linearly among these signal-coarse region. This interpolation method effects increase of the cut-off frequency in the artifact region.

2 METHODS

2.1 Data Acquisition

Retinal signal is acquired from rd1 mice after potential 10 week. The method used in Steet *et al.* (2000) is modified for retinal preparation. The eyeball is enucleated and the retina is isolated. From the isolated mouse retina, ganglion cell side of a retinal segment (approximately 5×5 mm^2) is attached on the surface of the 8×8 multi-electrode arrays (Multi Channel Systems GmbH, Germany). The RGC responses are extracellularly recorded with 8×8 multi-electrode array in which one electrode is used as stimulating electrode and all other electrodes as recording electrode (Stett et al., 2000). We apply electrical stimulation that is cathodic phase-first biphasic current pulses (square pulse) in every 1 sec 50 times. Its pulse duration is 500 µs and pulse amplitude is varying from 5 µA to 60 µA. The RGC activities are recorded by MC Rack (Multi Channel Systems GmbH, Germany).

2.2 Data Analysis

Concisely, we subtract the recorded raw signal by the filtered signal using adaptive FR filter. The subtracted signal is thresholded and clustered. Filtering, subtracting, and clustering are programmed by MATLAB (Mathworks, U.S.A.).

In detail, our first process is depegging. The recorded RGC signal includes minimum or maximum values by stimulation. This saturation has no RGC response information. Therefore, we convert saturation values into zero. This technique is called depegging following the previous report (Wagenaar and Potter, 2002). The maximum value is evoked after the minimum value because we use cathodic phase-first biphasic current pulse (square pulse) as stimulus pulse. Therefore, the depegging interval is decided from stimulus time to ninety percent of anodic saturation value. After the original data are depegging, the adaptive FR filter algorithm is applied.

2.2.1 FR Filter Algorithm

The FR filter stands for ‘forward-reverse filter’. The FR filter algorithm performs zero-phase filtering by filtering the raw signal in both the forward and the reverse directions with the identical time invariant filter. The main effect of the FR filter is elimination of phase distortion (Gustafsson, 1994).

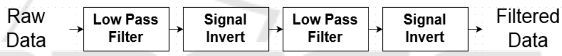

Figure 1: The flow chart of the basic FR filter algorithm.

We apply 3rd order Butterworth high-pass filter with 100 Hz cut-off frequencies for base-line smoothing before the FR filtering. The FR filter algorithm is operated with 3rd order Butterworth low-pass filter. We apply 500 Hz cut-off frequencies because the peak frequency of most spikes is somewhere around 625 Hz (Jin et al., 2005). After that, we subtract the results of the FR filter algorithm from the results of the 100 Hz high-pass filter. However, the FR signal does not effectively remove residual artifact because along the time axis the recorded voltage is varied dramatically. Therefore, we select over 1.6 ms waves, which start from 0 voltages and end in 0 voltages, as the residual artifact, because most spikes have showed 1.6 ms duration (Jin et al., 2005). The selected residual artifact is processed by our proposed interpolation method.

2.2.2 Interpolation Method

We linearly interpolate two points between the recorded signals at the selected residual artifact. This means that the number of signal increases 3 times by the interpolation. The interpolated signal is operated by low pass FR filter algorithm with 500 Hz of the cut-off frequencies. After filtering, values at the interpolated times are removed. This removal accomplishes that the interval between values are restored to the status before the interpolation. This restored signal is attached at the original time. This interpolation method effects to increase the cut-off frequency of the FR filter algorithm at the selected residual artifact.

2.3 Performance Evaluation of the Adaptive FR Filter

2.3.1 Comparison Data

We compare the adaptive FR filter with and without the proposed interpolation method. As a reference, they were compared with other researchers' work, the Subtraction of Artifacts by Local Polynomial Approximation (SALPA) (Choi et al., 2015; Wagenaar and Potter, 2002).

The SALPA algorithm is a stimulus artifact removal filter using locally fitted cubic polynomials, designed by Daniel Wagenaar and Steve Potter. A model of the artifact based on locally fitted cubic polynomials is subtracted from the recorded original signal. The algorithm yields a flat baseline amenable to spike detection by threshold voltage (Wagenaar and Potter, 2002).

2.3.2 Receiver Operating Characteristics Analysis

In order to evaluate the proposed adaptive FR filter, we use receiver operating characteristics (ROC) analysis. The ROC analysis is useful for organizing classifiers and visualizing their performance. The ROC classified into four groups; the true positive, the true negative, the false positive, the false negative (Fawcett, 2006). Table 1 shows a confusion matrix.

Table 1: The two-by-two confusion matrix.

		Actual Class	
		Yes	No
Predicted Class	Yes	True Positive	False Positive
	No	False Negative	True Negative

We evaluate and compare filters in point of the first spike detection performance after the stimulus. In our experimental experience, most spikes have been detected after 4 ms from the stimulus time. Based on our experimental experience, spike detection before 4 ms means the false positive. No spike detection before 4 ms is the true negative. In order to categorize the true positive and the false negative, we compared the first spike time of the adaptive FR filter, the simple FR filter, and the SALPA. If one filter detected first spike after 4 ms earliest, that filter is regarded as the true positive performance. If other filter algorithm detected its own first spike within 2 ms follow the first filter algorithm, that algorithm is considered as the true positive also. The 2 ms tolerance is allowed because most spike showed approximately 2 ms duration time. If other filter algorithm detected its own first spike in 2 ms later than the first spike, that algorithm is regarded as the false negative. We plotted the ROC graph which locates the true positive rate (TP rate) on the Y axis and the false positive rate (FP rate) on the X axis.

The true positive rate is estimated as

$$\text{TP rate} \approx \frac{\text{true positive}}{\text{true positive} + \text{false negative}} \tag{1}$$

The false positive rate is estimated as

$$\text{FP rate} \approx \frac{\text{false positive}}{\text{true negative} + \text{false positive}} \tag{2}$$

This ROC graph enables to compare 3 filters' performance and threshold value. Therefore, we varied the threshold time for the first spike criteria from 1 ms to 7 ms in order to evaluate our experimental experience, 4 ms.

3 RESULTS

3.1 Short-latency Spike Detection

The adaptive FR filter using the interpolation method detects the short-latency spike that has been obscured by the artifact slope (Figure 2 and 3).

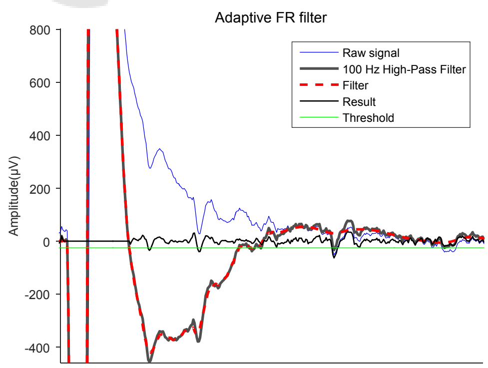

Figure 2: The raw signal (the blue solid line) is filtered by 100 Hz high pass filter for the base line smoothing (the grey line). The high pass filtered signal is processed by the adaptive FR filter (the red dotted line). The final result (the black line) which subtracts the red dotted line from the grey line is discriminated from noise by threshold (the green line).

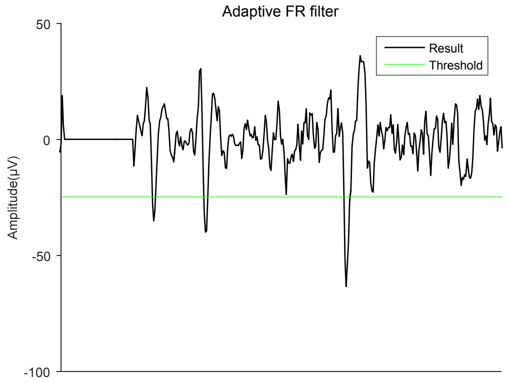

Figure 3: The subtracted signals (the black line) is distinguished by the threshold (the green line). Three short-latency spikes are detected.

3.2 Receiver Operating Characteristics Analysis

3.2.1 True Positive Rate

Comparing to the three algorithms with respect to the true positive rate, the SALPA shows the best performance as 0.8136, and the simple FR filter show the worst performance as 0.7546.

Table 2: Comparison the true positive rate of three algorithms.

	Adaptive FR filter	Simple FR filter	SALPA
0 ms	0.7319	0.6733	0.7508
1 ms	0.7319	0.6733	0.7508
2 ms	0.7319	0.6731	0.7510
3 ms	0.7325	0.6750	0.7527
4 ms	0.7629	0.6881	0.7541
5 ms	0.7632	0.7236	0.7800
6 ms	0.7485	0.7525	0.8107
7 ms	0.7770	0.7546	0.8136

3.2.2 False Positive Rate

Table 3: Comparison the false positive rate of three algorithms.

	Adaptive FR filter	simple FR filter	SALPA
0 ms	0	0	0
1 ms	0	0	0
2 ms	0	0.0002	0
3 ms	0.0028	0.0014	0.0006
4 ms	0.0047	0.0184	0.0329
5 ms	0.0625	0.0447	0.0707
6 ms	0.1570	0.0950	0.1272
7 ms	0.1944	0.1535	0.1899

Comparing to the three algorithms with respect to the false positive rate, the SALPA shows the best performance at 0 ~ 3 ms threshold. After 3 ms, however, the false positive rate of the SALPA increases rapidly.

3.2.3 Roc Graph

Considering all the results, the threshold of the adaptive FR filter, the simple FR filter, and the SALPA for the best performance are 4 ms, 5 ms, and 3 ms, respectively. The proposed algorithm shows the best true positive rate as 0.7629 comparing with the SALPA (0.7527) and the simple FR filter (0.7236) without the interpolation method. In point of view of the false positive rate, the proposed algorithm demonstrates the second-best performance as 0.0047. The best false positive rate is the SALPA (0.0006). Figure 4 shows the ROC graph of three algorithms at best performance threshold time.

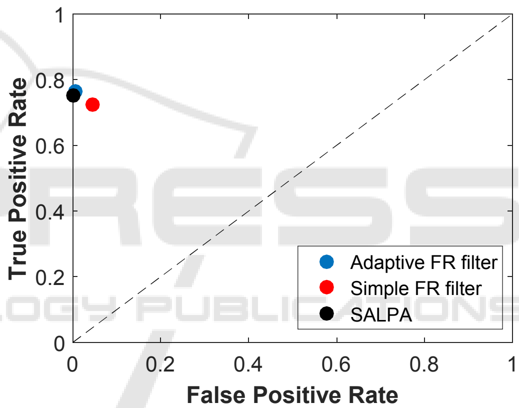

Figure 4: Comparison of the three algorithms using ROC graph.

As seen in Figure 4, the adaptive FR filter and the SALPA had similar performance. On the other hand, the simple FR filter is poor performance comparing with other algorithms.

4 CONCLUSIONS

The adaptive FR filter effectively removes the artifact and successfully isolates the short-latency spike from the artifact slopes. In the ROC graph, the adaptive FR filter shows good performance with the SALPA. It is much better performance than that of the simple FR filter. We have plan to apply the neural network algorithm in order to enhance the performance of the adaptive FR filter.

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