An improved masker-probe method for stimulus artifact reduction in electrically evoked compound action potentials

Isaac Alvarez [a] Angel de la Torre [a] Manuel Sainz [b,c]
Cristina Roldan [c] Hansjoerg Schoesser [d] Philipp Spitzer [d]

[a] *Department of Signal Theory, Telematics and Communications, University of Granada, Spain*

[b] *Department of Surgery and its Specialities, University of Granada, Spain*

[c] *ENT Service, San Cecilio University Hospital, Granada, Spain*

[d] *MED-EL Medical Electronics, Innsbruck, Austria*

Abstract

The masker-probe paradigm is a commonly used technique to reduce stimulus artifact in electrically evoked compound action potential registers. This method takes advantage of the refractory properties of the cochlear nerve, combining the responses to different types of stimulation pulses in order to obtain the biological response free of artifact. In this paper we extend the masker-probe paradigm by combining the responses to these stimulation pulses with optimal weights. We also provide an automatic method to obtain an estimation of the optimal weights. A comparison with the conventional masker-probe paradigm shows that the proposed method improves the quality of electrically evoked compound action potential registers.

Key words: Electrically Evoked Compound Action Potential (ECAP), stimulus artifact reduction, masker probe paradigm.

1 Introduction

Most modern cochlear implant systems allow the electrically evoked compound action potential (ECAP) to be recorded (Brown, 1998; Dillier, 2002; Frijns, 2002; Zierhofer, 2003). They include a subsystem that provides a stimulation pattern at certain electrodes and records the electrical activity at others. These measurements represent the compound action potential associated with the synchronous firing of the neurons in the spiral ganglion evoked by electrical stimulation. The typical neural response waveform is characterized by a negative peak N1 (with a latency of 200-400 μs) followed by a positive peak P2 (with a latency of 500-700 μs). Such evoked potentials provide an assessment of auditory nerve status (Miller, 1994) and may assist the clinician in fitting the cochlear implant speech processor (Hughes, 2000; Franck, 2001; Smoorenburg, 2002; Brown, 2003; Polak, 2005).

Because the recording electrode is located in the cochlea, it produces relatively robust response amplitudes and is largely immune from contamination by muscle activity. However, because of its short response latency and close proximity to the stimulation electrode, the ECAP suffers from a relatively large amplitude stimulus artifact that overlaps temporally with the neural response (Miller, 2000). This artifact, caused by the stimulus applied to evoke the response, consists of a peak followed by an exponential decay (Martin, 2004; Spitzer, 2006). Additionally, the stimulus artifact is synchronous or coherent with the stimulation pulse and cannot be removed by the conventional technique of ensemble averaging.

Methods used to reduce stimulus artifact in ECAP recordings typically involve manipulations of the stimulus. One of the most commonly used methods is the masker-probe paradigm (Brown, 1990; Miller, 2000). This method takes advantage of the refractory properties of the cochlear nerve, reducing stimulus artifact by subtracting a "template" of the stimulus artifact from the recorded response, which contains both the stimulus artifact and the neural response. This template is achieved by presenting a masking pulse a short interval before presenting the probe stimulus pulse. The evoked potential is measured after the probe pulse is presented. Appropriate selection of the masker-probe interval is essential, because the nerve must be unresponsive to the probe stimulus. Since this template also contains the tail-end of the ECAP response to the masker pulse, the recorded response to the masker presented alone is also recorded and added back to the previous subtraction to cancel out the response to the masker. Thus, after this manipulation the masker-probe paradigm provides an estimation of the ECAP response free of stimulation artifact. However, the method relies on the linearity of the system, which is not generally verified (Geddes, 1997; Ragheb, 1990). In addition, this masker-probe method can distort the ECAP waveform when the stimulated nerve is in a condition of partial refractoriness (Finley, 1997; Abbas, 2003) due to the distribution of refractory periods (Sainz, 2005).

In this work we extend the masker-probe paradigm in order to deal with the limitations associated with this technique. Based on an automatic method that assesses the quality of an ECAP response described in a previous paper (Alvarez, 2007), we propose a generalized masker-probe method. This new method combines the responses to the stimulation pulses involved in the masker-probe paradigm with optimal weights. These optimal weights are calculated as those that maximize the quality of the evoked response and therefore those that minimize the stimulus artifact.

This paper is organized as follows. Section 2 describes the data acquisition procedure for ECAP recording. Section 3 describes the conventional and generalized masker-probe methods. In section 4 we analyze the improvement provided by the proposed method, including comparisons with other artifact reduction methods. Finally, section 5 summarizes the main contributions and conclusions.

2 ECAP Acquisition

The ECAP responses used in this study were recorded from 50 patients, with a wide age range (from 6 months to 74 years). All patients were implanted with the Med-El Pulsar CI^{100} cochlear implant (Zierhofer, 2003; Schoesser, 2005; Spitzer, 2006). This implant's ECAP recording system allows different configurations to be used for stimulation and recording. The stimulation configuration used in this study was set up in masker-probe mode. This mode acquires four registers corresponding to four different stimulation patterns. Figure 1 shows the stimulation patterns for obtaining each register: S_a, S_b, S_c and S_d. In order to obtain each register, we averaged 50 responses for each stimulation pattern by the conventional ensemble-averaging method. The stimulation rate used was 50 Hz (a response was recorded every 20 ms). The first biphasic pulse of the stimulation patterns is the masker and the second one is the probe pulse. The "Inter Pulse Interval" (IPI) represents the time interval between the two pulses. In this study, we used an IPI of 0.5 ms. Biphasic pulses were set up with durations of each phase between 30 and 45 μs, and amplitudes under 1200 μA.

Each prospective subject was given an informed-consent form explaining the purpose and procedures involved in the study. If the patient agreed to participate, the form was signed and the subject was provided with a copy. The experimental protocol was approved by the Ethic Committee of San Cecilio University Hospital, Granada (Spain).

3 Masker-probe paradigm

3.1 Registers associated with the different stimulation patterns

The ECAP recording system allows four types of registers involved in the masker-probe mode to be recorded: R_a, R_b, R_c and R_d (corresponding to the stimulation patterns S_a, S_b, S_c and S_d described in figure 1). Assuming the linearity of the system, we can describe the register R_a corresponding to the stimulation pattern S_a (containing only the probe pulse) as:

$$R_a \approx A_p + B_p \tag{1}$$

where A_p and B_p are the artifact and the biological response corresponding to the probe pulse, respectively.

Register R_b contains the artifacts associated with the masker and probe pulses (A_m and A_p) and the biological response associated with the masker pulses (B_m). Since the IPI (0.5 ms) is smaller than the refractory period of the fastest neurons (Brown, 1990a, 1994; Sainz, 2005), the neurons remain in a refractory state when the probe pulse is presented, owing to the masker, and register R_b does not contain the biological response of the probe pulse:

$$R_b \approx A_m + A_p + B_m \tag{2}$$

Register R_c contains the artifact and the biological response associated with the masker pulse (A_m and B_m, respectively):

$$R_c \approx A_m + B_m \tag{3}$$

Finally, register R_d contains the inverted artifact associated with the masker and probe pulses ($-A_m$ and $-A_p$) and the biological response to the masker pulses (B_m). As in the case of register R_b, since the IPI is short enough, register R_d does not contain the biological response to the probe pulse:

$$R_d \approx -A_m - A_p + B_m \tag{4}$$

3.2 Conventional masker-probe method

According to these definitions and assuming the linearity of the system, the conventional masker-probe register (R_{mp}) combines the registers R_a, R_c and R_b:

$$\begin{aligned} R_{mp} &= R_a - R_b + R_c \\ &= A_p + B_p - A_m - A_p - B_m + A_m + B_m \\ &= B_p \end{aligned} \tag{5}$$

and therefore the method provides the biological response to the probe pulse free of artifact.

Figure 2 shows an instance of an ECAP register obtained using the masker-probe method (R_{mp}). Registers R_a, R_b and R_c are also shown. We can observe that this method provides better quality than recording the evoked potential with a single stimulation pulse (i.e. a more consistent identification of waves N1 and P2 and a flatter behavior after wave P2). Therefore, the conventional masker-probe paradigm allows the stimulation artifact in electrically evoked compound action potentials to be reduced.

3.3 Generalized masker-probe method

Limitations associated with the conventional masker-probe paradigm (including non linearities due to the electrode-tissue interface, the recording system, etc. (Geddes, 1997; Ragheb, 1990) and distortions of the ECAP waveform when the stimulated nerve is in partial refractoriness (Finley, 1997; Abbas, 2003)) make the conventional masker-probe paradigm sub-optimal for artifact reduction. In order to deal with the limitations associated with this technique, we propose a generalized masker-probe method that combines the registers R_a, R_b, R_c and R_d with optimal weights specifically calculated for each register. Two variants of the generalized masker-probe method are proposed, referred to as R_{gmpA} and R_{gmpB}. The generalized masker-probe register R_{gmpA} can be obtained as:

$$R_{gmpA} = R_a + k_1^A R_b + k_2^A R_c \tag{6}$$

where $\{k_1^A, k_2^A\}$ are the optimal weights calculated for each register. Since our aim is to obtain the biological response associated with the probe pulse (B_p), R_a cannot be altered and a weight equal to 1 must be applied in order not to distort the biological response. Additionally, R_b has been acquired with a small enough IPI (0.5 ms) to contain no biological response B_p.

For the second variant, we propose including the register R_d. Since this register has been acquired with an IPI of 0.5 ms, its use may assist in reducing the stimulation artifact without distorting the biological response. The generalized masker-probe register R_{gmpB} can be calculated as:

$$R_{gmpB} = R_a + k_1^B R_b + k_2^B R_c + k_3^B R_d \tag{7}$$

where $\{k_1^B, k_2^B, k_3^B\}$ are the optimal weights calculated for each register. In order to calculate the $\{k_1^A, k_2^A\}$ and $\{k_1^B, k_2^B, k_3^B\}$ weights, we propose the use of an expert-based automatic method that assesses the quality of an ECAP response (Q), as described in a previous paper (Alvarez, 2007). This method assesses the quality of an ECAP response in the range of 0-10. Due to the exponential behavior of the stimulus artifact (Martin, 2004; Spitzer, 2006), an ECAP register is considered to be ideal if (1) the waves N1 and P2 can easily be identified, (2) the amplitude, quantified as the difference between both peaks, can reliably be measured and (3) it presents flat behavior after the evoked potential (Alvarez, 2007).

Thus, the optimal values of the $\{k_1^A, k_2^A\}$ and $\{k_1^B, k_2^B, k_3^B\}$ weights are obtained as those that maximize the quality and therefore those that provide the best artifact reduction:

$$\{k_1^A, k_2^A\} = \underset{\{k_1', k_2'\}}{\text{argmax}}[Q(R_{gmpA}(k_1', k_2'))] \tag{8}$$

$$\{k_1^B, k_2^B, k_3^B\} = \underset{\{k_1', k_2', k_3'\}}{\text{argmax}}[Q(R_{gmpB}(k_1', k_2', k_3'))] \tag{9}$$

where k_1', k_2' and k_3' are weights for which Q is computed and $\{k_1^A, k_2^A\}$ and $\{k_1^B, k_2^B, k_3^B\}$ are the sets of weights $\{k_1', k_2'\}$ and $\{k_1', k_2', k_3'\}$ providing the highest quality in equations (8) and (9), respectively. Note that the conventional masker-probe paradigm is a particular case of the generalized masker-probe-A technique with $\{k_1^A, k_2^A\}$=$\{-1, 1\}$ and of the generalized masker-probe-B technique with $\{k_1^B, k_2^B, k_3^B\}$=$\{-1, 1, 0\}$. The optimal weights were explored within an interval of ± 0.5 around the conventional values, i.e. $k_1' \epsilon [-1.5, -0.5]$, $k_2' \epsilon [0.5, 1.5]$ and $k_3' \epsilon [-0.5, 0.5]$.

The automatic quality assessment procedure includes a normalization, and the quality therefore depends on the response shape but not the amplitude (Alvarez, 2007). This prevents the proposed artifact reduction method from artificially increasing the ECAP amplitudes as a consequence of the quality optimization.

4 Comparison of generalized masker-probe method with other methods

In order to study the benefit of the proposed generalized masker-probe method, we have compared the quality of 122 ECAP registers acquired with the following artifact reduction methods:

- Conventional alternating stimulation. This method provides a response that is obtained as the average of recordings using anodic-cathodic and cathodic-anodic biphasic pulses as stimulation (Eisen, 2004). This method relies on the linearity of the system to reduce stimulus artifact and preserve the biological response.

- Generalized alternating stimulation. In a previous paper we extended the concept of alternating stimulation (Alvarez, 2007). Instead of using similar weights, 0.5 for anodic-cathodic and 0.5 for cathodic-anodic stimulation pulses, they are combined using different weights: α and $(1-\alpha)$ for anodic-cathodic and cathodic-anodic stimulation pulses, respectively. The optimal α value is automatically calculated as the one that maximizes the quality of the generalized alternating register.
- Conventional and generalized masker-probe methods. These methods have been calculated combining the S_a, S_b, S_c and S_d stimulation patterns (figure 1) according to equations 5 (conventional masker-probe method), 6 (generalized masker-probe-A method) and 7 (generalized masker-probe-B method).

Figure 3 shows four instances of ECAP registers acquired with these artifact reduction methods. The automatically estimated quality (Q) of each method is also indicated. Table 1 compares the quality (Q) provided by these artifact reduction methods for 122 ECAP registers, including the mean of the automatically estimated quality and its standard deviation. Mean and standard deviation of α, k_1, k_2 and k_3 weights are also shown. Our results indicate that the proposed techniques provide the highest average quality. The relatively high standard deviation of the optimal weights shows that the optimization specific for each ECAP recording is important for artifact reduction. The quality improvement with respect to conventional masker-probe is assured by the method, as the optimal values of the $\{k_1^A, k_2^A\}$ and $\{k_1^B, k_2^B, k_3^B\}$ weights are selected with a quality criterion and conventional masker-probe is a particular case of both generalized masker-probe-A and masker-probe-B methods. However, improvement is also achieved with respect to conventional and generalized alternating stimulation methods. These results also indicate that the previously proposed generalized alternating stimulation (Alvarez, 2007) provides better quality responses than the conventional masker-probe paradigm. In order to analyze the statistical significance of the improvement achieved by the proposed generalized masker-probe techniques with respect to the others, matched pair Student t-test was applied. Table 2 shows the p-values (probability of the null hypothesis that both the methods compared provide the same quality). We can observe that the improvement provided by generalized masker-probe-A technique with respect to the conventional masker-probe paradigm is statistically significant (p <0.05). Moreover, improvements with respect to conventional alternating and generalized alternating stimulation methods are statistically significant. Improvements with the generalized masker-probe-B technique with respect to all the other methods are also statistically significant.

Although the generalized masker-probe-B is the technique providing the best results, the computational load should be taken into account. In order to apply generalized alternating stimulation, the optimal α values have been automatically calculated using a MATLAB two-stage implementation running on a laptop computer with an Intel Core Duo CPU at 1.86 GHz. The first stage calculates the quasi-optimal α value with a step of 0.05 in the interval [0,1]. The second stage then calculates the optimal α value with a step of 0.005 in the interval of width 0.1 centered at the quasi-optimal α value. Computations of the quality in order to obtain the optimal α value for one recording take around 36 milliseconds. The weights used in the generalized masker-probe method have been automatically calculated using a similar two-stage algorithm (i.e. $k_1' \epsilon [-1.5, -0.5]$, $k_2' \epsilon [0.5, 1.5]$ and $k_3' \epsilon [-0.5, 0.5]$). The computation of the $\{k_1^A, k_2^A\}$ weights for generalized masker-probe-A takes 0.72 seconds on average. Thus, the time increments associated with the generalized alternating stimulation method and generalized masker-probe-A technique are reasonable, since they are smaller than the acquisition time (2 seconds and 3 seconds for generalized alternating stimulation and generalized masker-probe-A, respectively). However, computation of the $\{k_1^B, k_2^B, k_3^B\}$ weights for generalized masker-probe-B takes around 14.4 seconds and the acquisition time associated with this method is 4 seconds. Although computation using a compiled version would provide shorter processing times, the time increment of the generalized masker-probe-B technique with respect to the generalized masker-probe-A technique should be noted.

5 Conclusions

This work proposes an improved masker-probe approach to deal with the problem of the stimulus artifact in Evoked Compound Action Potentials recordings. The proposed method is a generalization of the conventional masker-probe paradigm. The conventional masker-probe method combines the responses to different types of stimulation pulses with fixed weights. Several effects (including non linearities and distortions of the ECAP waveform) make fixed weights sub-optimal for artifact reduction. Thus, we propose the generalized masker-probe-A and masker-probe-B techniques that combine the responses with optimal weights. Estimation of these weights is based on an automatic method that assesses the quality of an ECAP register, described in a previous paper. The optimal values of the weights are obtained as those that maximize the quality and therefore those that provide the best artifact reduction.

The proposed generalized masker-probe techniques have been compared with conventional alternating stimulation, generalized alternating stimulation and the conventional masker-probe paradigm over 122 ECAP registers. The results indicate that the proposed generalized masker-probe methods provide the best quality, with average quality increments of 2.92 and 3.70 units for generalized masker-probe-A and masker-probe-B techniques, respectively, with respect to the conventional masker-probe paradigm. Although the generalized masker-probe-B technique provides better quality than the generalized masker-probe-A technique, it should be noted that the computational load is greater.

Method	N	μ_Q	σ_Q	μ_α	σ_α	μ_{k_1}	σ_{k_1}	μ_{k_2}	σ_{k_2}	μ_{k_3}	σ_{k_3}
Conventional alternating	122	3.56	3.07	0.5	0	-	-	-	-	-	-
Generalized alternating	122	6.55	2.97	0.39	0.22	-	-	-	-	-	-
Conventional masker-probe	122	4.48	3.16	-	-	-1	0	1	0	0	0
Generalized masker-probe-A	122	7.40	2.69	-	-	-1.09	0.20	0.90	0.35	0	0
Generalized masker-probe-B	122	8.18	2.42	-	-	-1.08	0.23	0.92	0.37	0.01	0.35

Table 1
Comparison of different methods of artifact reduction for 122 ECAP registers. The mean and standard deviation of Q (μ_Q and σ_Q, respectively) are shown. The mean and standard deviation of α, k_1, k_2 and k_3 weights are also indicated.

	p-values (N=122)			
Methods	alt	mp	galt	gmpA
mp	3.42e-5			
galt	3.12e-13	1.62e-12		
gmpA	4.82e-29	8.44e-27	1.10e-3	
gmpB	2.11e-33	1.11e-30	1.40e-9	1.84e-2

Table 2
p-Values provided by matched pair Student t-test when comparing different artifact reduction methods for 122 ECAP registers.

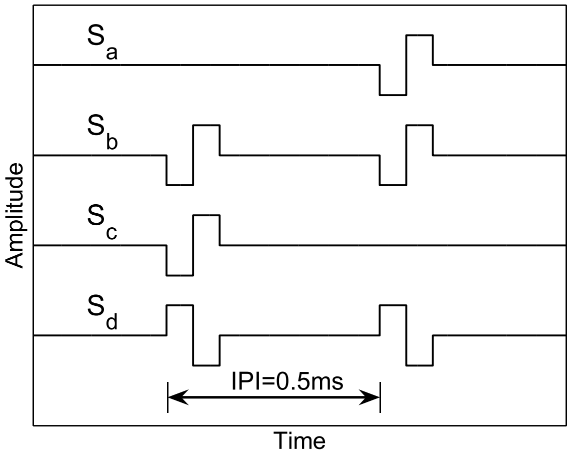

Fig. 1. Four stimulation patterns associated with the masker-probe paradigm.

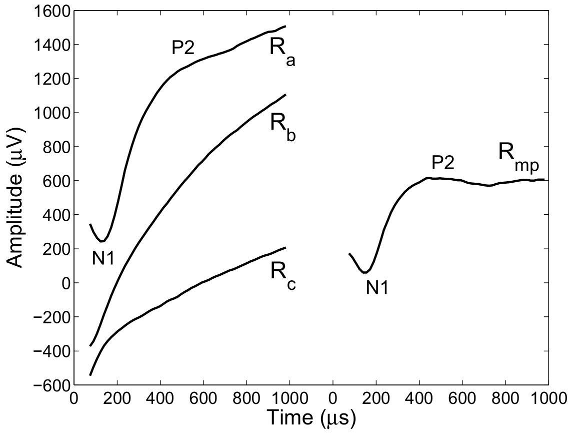

Fig. 2. Instance of registers associated with the masker-probe paradigm. R_{mp} represents the masker-probe register, $R_{mp} = R_a - R_b + R_c$.

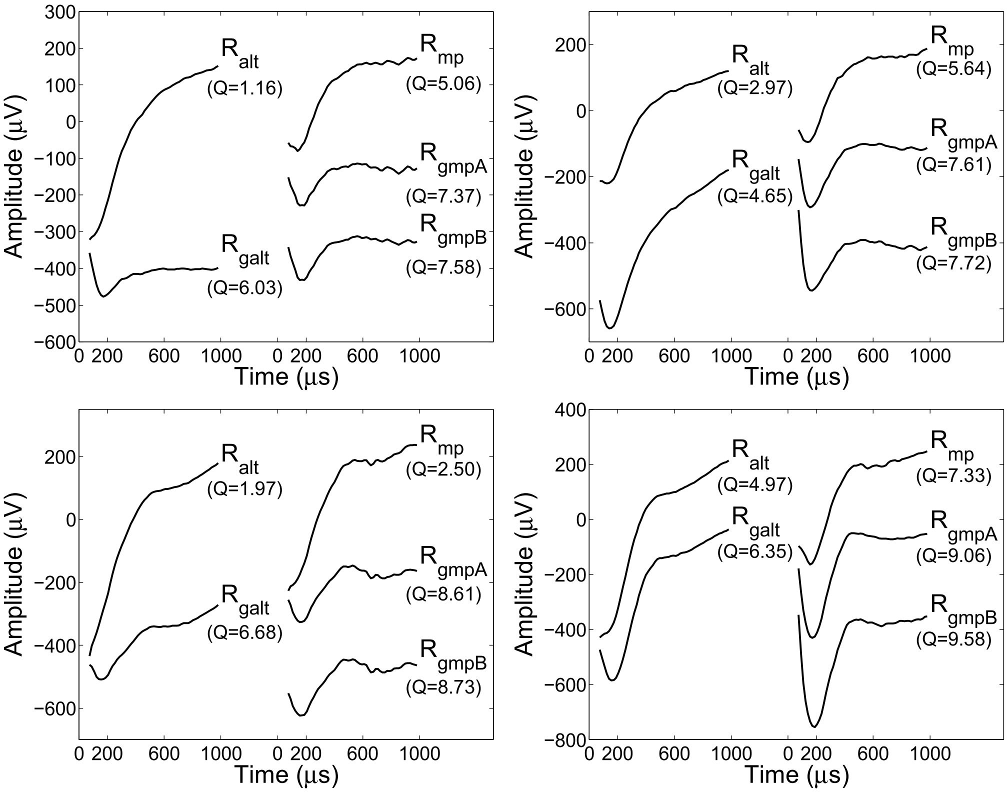

Fig. 3. Four ECAP registers acquired with conventional alternating stimulation (R_{alt}), generalized alternating stimulation (R_{galt}), conventional masker-probe paradigm (R_{mp}) and the proposed generalized masker-probe-A (R_{gmpA}) and masker-probe-B (R_{gmpB}) techniques. The automatically estimated quality (Q) for each method is also shown.

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