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**Generalized alternating stimulation: a novel  
method to reduce stimulus artifact in  
electrically-evoked compound action  
potentials**

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**Abstract**

Stimulus artifact is one of the main limitations when considering electrically-evoked compound action potential for clinical applications. Alternating stimulation (average of recordings obtained with anodic-cathodic and cathodic-anodic bipolar stimulation pulses) is an effective method to reduce stimulus artifact when evoked potentials are recorded. In this paper we extend the concept of alternating stimulation by combining anodic-cathodic and cathodic-anodic recordings with a weight in general different to 0.5. We also provide an automatic method to obtain an estimation of the optimal weights. Comparison with conventional alternating, triphasic stimu-

lation and masker-probe paradigm shows that the generalized alternating method improves the quality of electrically evoked compound action potential responses.

*Key words:* Electrically Evoked Compound Action Potential, stimulus artifact reduction, quality assessment, Gaussian Mixture Model, alternating stimulation, triphasic stimulation, masker-probe paradigm.

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## 1 Introduction

Most modern cochlear implant systems include a sub-system for recording electrically evoked compound action potentials (ECAPs). This subsystem provides a stimulation pattern at certain electrodes and records the electrical activity at some other electrode. The recording system integrated into the implantable device includes the amplification of the input signal, analog-to-digital conversion, encoding, storage and data transfer to an external system, where recorded data can be processed (Brown, 1998; Dillier, 2002; Frijns, 2002).

The recording system is intended to measure the compound action potential associated with the synchronous firing of the neurons in the spiral ganglion evoked by the electrical stimulation. However, in addition to the compound action potential, recordings also contain artifact coming from different sources. Two different kinds of artifact can be considered: random artifact and synchronized artifact. The random artifact has various possible origins, such as neural or muscular activity of the subject, external electrical interference or internal noise in the acquisition sub-system. The random artifact can be effectively reduced with the well-known ensemble averaging method, by averaging a number of responses (Regan, 1989). The synchronized artifact is mainly due to the stimulus applied to evoke the response. Typically, the stimulus artifact

is a peak followed by a decay response whose amplitude and time constant depend on the type of stimulation pulses, electrical properties of the tissues, electrode design and the filtering characteristics of the preamplifier stage of the recording system.

Stimulus artifact is an important source of distortion in ECAP recordings since the stimulation pulses require voltages typically in the range of 1-5 V and the smallest ECAP value that can reliably be measured has an amplitude of about 100  $\mu\text{V}$  (Eisen, 2004). Stimulus artifact is synchronous or coherent with the stimulation pulses and cannot be removed by ensemble averaging. In addition, stimulus artifact overlaps the evoked response in both the time and frequency domains, such that conventional time windowing and frequency filtering are incapable of removing stimulus artifact without distorting the evoked response.

The most commonly used methods to reduce stimulus artifact in ECAP recording are based on different types of stimulation pulses. Of these approaches, three techniques are particularly worthy of mention:

- The masker probe paradigm (Brown, 1990; Miller, 2000) takes advantage of the refractory properties of the cochlear nerve. The response is obtained by combining three different stimulus pulses: the masker pulse (presented at the start of the measurements), the probe pulse (presented after a short delay) and the masker-probe pulse (consisting in both pulses). With the nerve in a refractory state due to the masker, the recording corresponding to the masker-probe pulse consists of the stimulus artifact and a portion of response to the masker stimulus. This template is subtracted from the original response to the probe pulse. The recorded response to the masker alone is added to the previous subtraction to cancel the response to the masker in

the masker-probe pulse. This method therefore relies on the linearity of the system to obtain the biological response to the probe pulse. One of the main disadvantages of this method is that more measurements are necessary for each result. Additionally, the condition for the success of the method, that all nerves must be in a refractory state, is hardly ever met.

- Various authors have shown that the residual charge can be reduced by introducing a third phase to the stimulus (Schoesser, 2001; Frohne, 2005; Sainz, 2005). The effectiveness of this technique, based on stimulation with triphasic pulses, relies on the choice of the amplitude of the first phase relative to the second one. The amplitude of the third phase is automatically set in order to make the total charge introduced into the cochlea equal to zero and minimize stimulus artifact. Setting up the optimal percentage between the first and second phases is a difficult task that depends on several factors (including stimulation level, stimulated and measured electrode, etc.). Thus, setting up the optimal percentage requires expert supervision. One additional disadvantage of this method is that because of the third phase the first minimum (wave N1) of the ECAP signal may not register.
- Alternating stimulation (Eisen, 2004) provides a response that is obtained as the average of recordings using anodic-cathodic (ak) and cathodic-anodic (ka) biphasic pulses as stimulation. Under this approach, the biological response is assumed to be independent of the polarity of the first phase of the stimulation pulse (i.e. similar for ak and ka stimuli), even though neural responses to each stimulus polarity are not necessarily equal in amplitude or latency (Miller, 2000) and it has been shown that the auditory nerve has polarity-dependent sensitivity and responds with polarity-dependent latency in cats and guinea pigs (Miller, 1998). On the other hand, the stimulation artifact is assumed to change its polarity when ak or ka pulses are

used. This method therefore relies on the linearity of the system to reduce stimulus artifact and preserve the biological response.

In this paper we extend the concept of alternating stimulation. Instead of using similar weights, 0.5 for  $a_k$  and 0.5 for  $k_a$  registers, they are combined using different weights:  $\alpha$  and  $(1 - \alpha)$  for the  $a_k$  and  $k_a$  registers, respectively. Non linearities due to the electrode-tissue interface, the recording system, etc. (Geddes, 1997; Ragheb, 1990) make 0.5 sub-optimal for artifact reduction. Thus, the  $\alpha$  weight can be selected in order to minimize stimulus artifact, and this generalized alternating method can provide better artifact reduction than the conventional alternating method. Note that  $a_k$ ,  $k_a$  and conventional alternating responses are particular cases of the generalized alternating method for  $\alpha = 1$ ,  $\alpha = 0$  and  $\alpha = 0.5$ , respectively.

For the selection of the optimal value of  $\alpha$ , an automatic method is desirable, in order to avoid supervised processing of the ECAP responses and to provide a systematic procedure when the ECAP responses are used for research and clinical applications. In this paper we propose an automatic method for the estimation of  $\alpha$ . Estimating  $\alpha$  relies on an automatic assessment of the quality of the ECAP responses. The automatic assessment of the quality is based on a Gaussian Mixture Model, generated from a set of supervised ECAP responses (Botros, 2006). This method provides an automatic assessment of the quality for a new input response. Finally, the optimal value of  $\alpha$  is selected as the one providing the highest quality.

The rest of the paper is organized as follows. Section 2 describes data acquisition procedure for ECAP recording. Section 3 describes the conventional and generalized alternating methods, and analyzes the potential improvement that

can be achieved by the generalized alternating method over a set of ECAP responses supervised by an expert. Section 4 presents the procedure for the automatic assessment of quality and some validation experiments. In section 5 we present validation experiments for the proposed method to automatically calculate the optimal value of  $\alpha$ . In section 6 we analyze the improvement provided by the generalized alternating method over a set of unsupervised ECAP responses, including comparisons with conventional alternating stimulation, masker-probe paradigm and triphasic methods. Finally, main contributions and conclusions are summarized in section 7.

## 2 Data acquisition and data reduction

In this section we describe the hardware used for recording the ECAP responses and its configuration. We also describe the data reduction process applied to represent each register.

### 2.1 Data acquisition

ECAP responses have been recorded from cochlear implant users wearing the MedEl PULSARCI<sup>100</sup> device (Schoesser, 2005). This cochlear implant system includes an ECAP Recording System which allows different types of stimuli to be presented at some electrodes and allows the evoked response (recorded at some other electrode) to be stored in an internal memory. By means of a telemetry system the collected data are transferred to an external system for subsequent processing. The ECAP registers used in this study were recorded from 59 patients, with a wide age range (from 6 months to 74 years). The

ECAP Recording System allows different configurations to be used for stimulation and recording. The stimulation pattern used in this work has been set up in alternating mode, using ak and ka biphasic pulses, with durations of each phase of between 30 and 45  $\mu\text{s}$ , and amplitudes under 1200  $\mu\text{A}$ .

## 2.2 Data reduction

ECAP recordings are achieved with a blanking amplifier (input of the amplifier is in short-circuit for 125  $\mu\text{s}$  after the beginning of the stimulation pulse). An adaptive  $\Sigma\Delta$  modulator, at  $f_s=1.2\text{MHz}$ , converts the signal from analog to digital (Zierhofer, 2000; Gray, 1987). Each recording is a sequence of 2048 bits (representing a register of approximately 1.7 ms). The demodulation of the signal generates a prediction signal to obtain a multilevel recovered signal. Since the signal is over-sampled by a factor of  $R$ , a low pass filter with cut-off frequency of  $(1/R) \cdot f_s$  can be applied to average the last  $R$  samples in order to recover the signal. The recovered signal can then be under-sampled by taking one of each  $R/2$  samples. Thus, each response can be efficiently represented with 102 samples at a sampling frequency of 60 kHz ( $R=40$ ). Considering only the time interval where the evoked response is present (approximately 70-980  $\mu\text{s}$ ), each evoked response is a vector of only 57 samples.

In the data acquisition performed in this study, for each recording we recorded 50 responses for each, ak and ka, bipolar stimulation modes. After representing each response as a 57 components vector, the ak and ka vectors were averaged. Thus, for each recording (initially represented as 50 ak and 50 ka sequences of 2048 bits) we obtain two 57-component vectors, one to represent the ak response and the other for the ka response.



### 3 Conventional and generalized alternating stimulation

In order to study the potential benefit of the generalized alternating method, we analyzed the effect of using a value of  $\alpha$  other than 0.5 on a database containing 102 ECAP recordings. The optimal value of  $\alpha$  was assigned to each recording by a researcher experienced in ECAP measurements obtained with different cochlear implant systems and also in other electrically evoked objective responses. We use  $\alpha_E$  to represent the value assigned by the expert. Figure 1 shows the distribution of  $\alpha_E$  for this supervised database. The distribution of  $\alpha_E$  presents a mean value and standard deviation of 0.42 and 0.22, respectively. Even though  $\alpha=0.5$  (conventional alternating) is a reasonable value for most recordings (better than  $\alpha=0$  or  $\alpha=1$ ), the best option would be a specific adaptation of  $\alpha$  to each ECAP recording.

Figure 2 represents four instances of ECAP registers (in these plots the amplitude has been normalized in order to allow comparisons). In each plot, the responses are represented for different values of  $\alpha$  ( $\alpha=0$  or ak stimulation;  $\alpha=1$  or ka stimulation;  $\alpha=0.5$  or conventional alternating stimulation; and  $\alpha=\alpha_E$  or generalized alternating method). When comparing the plots, we find that some recordings are greatly affected by the value of  $\alpha$ , while others are only slightly affected. We also observe how the artifact distorts the amplitude of the evoked response: sometimes the artifact reduces the amplitude (see register with  $\alpha=0$  in the bottom-left panel) and sometimes it increases it (see register with  $\alpha=0$  in the bottom-right panel). Additionally, the artifact reduction achieved with the  $\alpha$  proposed by the expert is better than that for the conventional alternating method.

We propose obtaining the optimal value of the  $\alpha$  weight as the one that provides the best artifact reduction and therefore the one that maximizes quality. The assignment of  $\alpha$  in the supervised database was performed by optimizing quality according to an expert criterion. In the next section we propose a novel method to obtain a measure of the quality ( $Q_A$ ) automatically. This method will be used later for the automatic calculation of the optimal  $\alpha$  value.

## 4 Automatic assessment of the quality in ECAP responses

### 4.1 Method description

Assessment of the quality of ECAP responses is based on a Gaussian Mixture Model or GMM (Zhuang, 1996; Hedelin, 2000; Falk, 2004; Dharanipragada, 2006). The GMM developed in this work is obtained from a set of  $K$  supervised registers  $\{\vec{x}_k\}$  ( $k = 1, 2, \dots, K$ ) each with a quality  $Q_k$  assigned by an expert. A Gaussian probability density function  $p(\vec{x}|k)$  is assigned to each supervised register. This way, the expected value of the quality  $Q$  for a new input register  $\vec{x}$  is obtained from this GMM as:

$$Q_A(\vec{x}) = E[Q(\vec{x})] = \sum_{k=1}^K Q_k P(k|\vec{x}) \quad (1)$$

where  $P(k|\vec{x})$  is the probability of each Gaussian  $k$  given the input vector  $\vec{x}$ , given by the Bayes rule:

$$P(k|\vec{x}) = \frac{p(\vec{x}|k)P(k)}{p(\vec{x})} \quad (2)$$

where  $p(\vec{x}|k)$  is the probability density function of the Gaussian  $k$  evaluated at the input vector  $\vec{x}$ ;  $P(k)$  is the a-priori probability of the Gaussian  $k$ ; and  $p(\vec{x})$  is the a-priori probability density of the input vector  $\vec{x}$ , which can be estimated in the GMM as:

$$p(\vec{x}) = \sum_{k=1}^K p(\vec{x}|k)P(k) \quad (3)$$

The probability  $P(k)$  can be considered equal for all the Gaussians (since each Gaussian comes from one supervised register). We may therefore consider  $P(k) = 1/K$ .

The general expression of the probability density function of the Gaussian  $p(\vec{x}|k)$  is:

$$p(\vec{x}|k) = \frac{1}{(2\pi)^{N/2}(|\Sigma_k|)^{1/2}} \exp\left(-\frac{(\vec{x} - \vec{\mu}_k)^t(\Sigma_k^{-1})(\vec{x} - \vec{\mu}_k)}{2}\right) \quad (4)$$

where  $\vec{\mu}_k$  is the mean of the Gaussian  $k$  ( $\vec{\mu}_k = \vec{x}_k$ );  $\Sigma_k$  is the covariance matrix of the Gaussian  $k$ ; the argument of the exponential is a matrix product;  $(\vec{x})^t$  represents the transposed of  $\vec{x}$ ;  $\Sigma_k^{-1}$  is the inverse of the matrix  $\Sigma_k$ ; and  $|\Sigma_k|$  is the determinant of  $\Sigma_k$ . Since all the Gaussians have been generated from a set of supervised vectors  $(\vec{x}_1, \vec{x}_2, \dots, \vec{x}_K)$ , the probability density functions can be simplified by considering spherical covariance matrices common to all the Gaussians. In this case, equation (4) can be expressed as:

$$p(\vec{x}|k) = \frac{1}{(2\pi\sigma^2)^{N/2}} \exp\left(-\frac{\|\vec{x} - \vec{x}_k\|^2}{2\sigma^2}\right) \quad (5)$$

where  $\sigma^2$  is the variance assigned to all the components of all the Gaussians.

With these considerations,  $Q_A(\vec{x})$  can be estimated as:

$$Q_A(\vec{x}) = \frac{\sum_{k=1}^K Q_k \exp\left(-\frac{\|\vec{x}-\vec{x}_k\|^2}{2\sigma^2}\right)}{\sum_{k=1}^K \exp\left(-\frac{\|\vec{x}-\vec{x}_k\|^2}{2\sigma^2}\right)} \quad (6)$$

The value of  $\sigma^2$  must be large enough to allow the set of supervised vectors  $(\vec{x}_1, \vec{x}_2, \dots, \vec{x}_K)$  to generalize quality estimate for a new input vector. On the other hand, it must be small enough not to smooth the quality estimate excessively. There is a trade-off between the generalization capability and the smoothing of the probabilities. In the limit when  $\sigma^2 \rightarrow 0$ , the quality assigned to the input vector is that of the nearest Gaussian:

$$\lim_{\sigma^2 \rightarrow 0} Q_A(\vec{x}) = Q_{kn} \quad \text{with} \quad kn = \min_{k=1..K}^{-1}(\|\vec{x} - \vec{x}_k\|^2) \quad (7)$$

and in the limit when  $\sigma^2 \rightarrow \infty$ , all the input vectors are assigned with the average quality:

$$\lim_{\sigma^2 \rightarrow \infty} Q_A(\vec{x}) = \sum_{k=1}^K Q_k \quad (8)$$

The optimal value of  $\sigma^2$  is the lowest value that remains generalization-capable and it depends on the dimensionality of the representation space ( $N$ ) and on the number of supervised vectors ( $K$ ) included in the definition of the quality. When  $N$  decreases, the distances  $\|\vec{x} - \vec{\mu}_k\|^2$  are smaller, and a smaller  $\sigma^2$  value can be used without losing generalization capability. When  $K$  increases, a smaller value of  $\sigma^2$  can be also used without losing generalization. Obviously, as the number of supervised vectors increases the automatic quality estimate becomes more consistent. However, the difficulties involved in supervising a large number of registers must also be taken into account. It is therefore rec-

commendable to reduce the number of dimensions  $N$  in the representation space.

Through Principal Components Analysis or PCA (Jackson, 1991) the dimensionality of the representation space can be reduced, keeping the best compromise between the number of components and the mean square error. The registers are approximated as:

$$\vec{x} \approx \sum_{n=1}^{N_B} b_n \vec{e}_n \quad \text{where} \quad b_n = \langle \vec{x}, \vec{e}_n \rangle \quad (9)$$

where  $\langle, \rangle$  denotes the inner product and  $\vec{e}_n$  ( $n = 1, \dots, N_B$ ) are the  $N_B$  first eigenvectors from the Principal Component Analysis. Thus, each register  $\vec{x}$  is represented by a set of  $N_B$  parameters  $\vec{b} = \{b_1, \dots, b_{N_B}\}$ , i.e. by a vector of  $N_B$  components. Finally, since the quality of a register is assessed according to the shape of the wave (rather than the amplitude), it is necessary to normalize the vectors:

$$\vec{B} = \frac{\vec{b}}{\|\vec{b}\|} = \frac{\vec{b}}{\sqrt{\langle \vec{b}, \vec{b} \rangle}} \quad (10)$$

In summary, the quality assigned to a new register  $\vec{x}$ , represented as a normalized vector  $\vec{B}$  with  $N_B$  coefficients, is based on a model of  $K$  Gaussians obtained from  $K$  supervised registers  $\{\vec{x}_k\}$  ( $k = 1, 2, \dots, K$ ) represented as  $K$  normalized vectors  $(\vec{B}_1, \vec{B}_2, \dots, \vec{B}_K)$ , each with a quality assigned by an expert  $(Q_1, Q_2, \dots, Q_K)$ . This quality is obtained as:

$$Q_A(\vec{x}) = \frac{\sum_{k=1}^K Q_k \exp\left(-\frac{\|\vec{B}-\vec{B}_k\|^2}{2\sigma^2}\right)}{\sum_{k=1}^K \exp\left(-\frac{\|\vec{B}-\vec{B}_k\|^2}{2\sigma^2}\right)} \quad (11)$$

## 4.2 Data description

In order to establish the set of Gaussians in the GMM, we used 102 recordings from 34 subjects (3 from each subject), acquired in alternating mode. For each recording, we have obtained 9 registers using  $\alpha = \frac{1}{8} \cdot i$  ( $i = 0, 1, \dots, 8$ ), with a total of 918 registers. After the data reduction described in section 2, registers  $\vec{x}$  are represented by a vector of 57 components, each corresponding to a sample, with a sample period of  $16.67\mu\text{s}$ . Through a reduction in the representation space, each vector is represented as a vector of 7 components ( $N_B=7$ ),  $\vec{B}_k$ . This process includes PCA (with a mean square error under 0.5%) and normalization of the vectors in the reduced representation space. The eigenvalues of the PCA performed over these 918 registers allow random vectors to be generated. Consequently, we extended the training database to 3000 vectors ( $K=3000$ ). Each vector has been assessed by the expert, assigning a quality in the range of 0-10. The assessment was performed by a single expert in order to obtain a consistent quality assignment. Additionally, the assessment criterion and the assignment of quality were supervised by several experts. The random extension of the training database aims to keep the number of registers uniform for each assigned quality.

The variance associated with the Gaussians for obtaining the quality automatically was set up with a value of  $\sigma^2 = 0.001$ , considering the value of the mean square distance between each vector and its nearest neighbor for the set  $(\vec{B}_1, \dots, \vec{B}_K)$ :

$$E[\|\vec{B}_k - \vec{B}_{n(k)}\|^2] = 0.00086$$

$$\text{where } n(k) = \min_{k' \neq k}^{-1}(\|\vec{B}_k - \vec{B}_{k'}\|^2) \quad (12)$$

Figure 3 shows instances of registers with different quality values assigned by the expert. An ECAP register is considered to be ideal if:

- It presents flat behavior after the evoked potential.
- The waves N1 and P2 can easily be identified.
- The amplitude can reliably be measured.

#### 4.3 Validation of the quality estimated automatically

In order to validate the proposed method for calculating the quality of an ECAP register automatically, we performed a linear regression analysis between the quality provided by the automatic method ( $Q_A$ ) and the quality assigned by the expert ( $Q_E$ ). Figure 4 represents  $Q_A$  versus  $Q_E$  for the 3000 ECAP vectors considered in the estimation of  $Q_A$  (training set). The qualities  $Q_A$  and  $Q_E$  are slightly different, due to the effect of smoothing associated with the use of a non-null variance (various ECAP training vectors contribute to the assigned value  $Q_A$ ). The linear regression analysis shows an evident statistical dependence ( $p < 1e-16$ ), and a high correlation coefficient ( $r=0.996$ ) between the expert and automatic quality estimates.

With a view to validating the proposed method,  $Q_A$  and  $Q_E$  were compared for a set of 75 new ECAP recordings. These recordings were obtained from 25 new subjects (different from those considered when generating the training database). Each recording was used to generate 9 ECAP registers, using  $\alpha = \frac{1}{8} \cdot i$  ( $i = 0, 1, \dots, 8$ ). The expert assigned a quality  $Q_E$  to each of these 675 registers. Figure 5 shows the linear regression analysis performed between the automatic quality,  $Q_A$ , and the quality assigned by the expert,  $Q_E$ , for these

675 registers.

The regression analysis indicates a clear statistical dependence between both quality estimates ( $p < 1e-16$ ). The correlation coefficient is also high ( $r=0.992$ ), although it is slightly lower than that for the training set. This high correlation between  $Q_A$  and  $Q_E$  over the validation set indicates that the automatic method proposed provides a consistent estimate of the quality of the registers.

## 5 Automatic optimization of $\alpha$

The quality estimate  $Q_A$  allows the optimal  $\alpha$  value to be calculated automatically. The optimal  $\alpha$  value is the one that maximizes the quality of the register  $\vec{x}_\alpha = (\alpha\vec{x}_{ak} + (1 - \alpha)\vec{x}_{ka})$ :

$$\alpha_A = \max_{\alpha}^{-1}[Q_A(\alpha\vec{x}_{ak} + (1 - \alpha)\vec{x}_{ka})] \quad (13)$$

and it can be estimated by calculating the quality  $Q_A(\vec{x}_\alpha)$  for a set of values of  $\alpha$  dense enough in the interval  $[0,1]$ .

In order to analyze the consistency of the proposed automatic procedure of optimization of  $\alpha$ , the values of  $\alpha_A$  and  $\alpha_E$  (provided by the automatic procedure and the expert, respectively) were compared. Figure 6 represents  $\alpha_A$  versus  $\alpha_E$  for the 102 ECAP recordings included in the training set (up) and for the 75 recordings included in the validation set (down). The regression analysis shows a significant statistical dependence for both estimates of  $\alpha$  ( $p < 1e-16$  in both cases) and high correlation coefficients ( $r=0.975$  for the training set and  $r=0.973$  for the validation set). In addition, the regression line ( $y = ax + b$ ) is near to the identity in both cases ( $a=0.97$  and  $b = 0.009$  for the training set



and  $a=0.94$  and  $b = 0.029$  for the validation set).

These results show that the automatic estimate of the weight  $\alpha_A$ , is consistent with the expert-based estimate. The automatic proposed method therefore provides a good estimate of the optimal  $\alpha$  value in the generalized alternating stimulation method.

## 6 Comparison of generalized alternating stimulation with other methods

The proposed generalized alternating method has been compared with conventional alternating, masker-probe paradigm and triphasic stimulation. Because of the time required to acquire masker-probe and triphasic pulses, more data is available for conventional alternating stimulation than for the other artifact reduction methods. For this reason, three different sets of recordings were defined for the comparisons: set A (including 2296 recordings in conventional alternating stimulation), set B (including 158 recordings obtained with the masker-probe paradigm) and set C (including 34 recordings with triphasic stimulation). Set A includes registers acquired in amplitude growth mode, with a stimulation level from  $0\mu\text{A}$  to a level close to the highest level comfortably tolerated by the patient. In sets B and C, the registers were acquired with a high stimulation level close to the highest level comfortably tolerated by the patient. Table 1 compares the quality provided by the different artifact reduction methods for these three sets, including average automatic quality and standard deviation. The proposed method is found to provide the highest average quality for the three sets of recordings. The quality improvement with respect to conventional alternating is assured by the method, as the op-

timal value of  $\alpha_A$  is selected with a quality criterion. However, improvement is also achieved with respect to masker-probe and triphasic pulse methods. It should also be noted that the quality improvement with generalized alternating compared with conventional alternating, masker-probe or triphasic pulses is similar to the improvement provided by these methods with respect to ak or ka stimulation.

In order to analyze the statistical significance of the improvement achieved by the proposed generalized alternating method with respect to the others, matched pair Student t-test was applied. The  $p$ -values (probability of the null hypothesis that the proposed and the reference method provide the same quality) are smaller than  $8e-14$  in both, set A and set B. The  $p$ -values in set C are higher because fewer registers were involved ( $p < 3e-4$ ). The quality improvement achieved with the proposed method is therefore statistically significant in the three sets of ECAP recordings ( $p < 0.05$ ).

Regarding the time increment associated with the proposed generalized stimulation method, it should be noted that the acquisition time is exactly the same as in the case of conventional alternating stimulation, since ak and ka recordings are necessary in both cases. In order to apply generalized alternating stimulation, the quality of the registers must be automatically assessed for different  $\alpha$  values. In the experiments performed in this study, we considered 241 values of  $\alpha$  in the interval  $[0, 1]$ . The computation of the quality for these 241 registers (in order to obtain the optimal  $\alpha$  for 1 recording) takes 675ms with a MATLAB implementation running on a laptop computer with a Pentium 4 CPU at 2.80GHz, which is a reasonable processing time (smaller than the acquisition time).

## 7 Conclusions

This work proposes a generalization of the alternating stimulation method in order to reduce stimulation artifact of Evoked Compound Action Potentials recorded in cochlear implant users. With the aim of minimizing the stimulus artifact, the recordings acquired with bipolar stimulation (anodic/cathodic and cathodic/anodic) are combined according to a weight  $\alpha$ . We also verified that, although the conventional method ( $\alpha=0.5$ ) of alternating stimulation provides an acceptable artifact reduction, the optimal  $\alpha$  value is not necessarily equal to 0.5 and for some recordings it can be very different.

An expert-based automatic method is also proposed in order to assess the quality of the ECAP responses. This method can be used to automatically obtain the optimal value of  $\alpha$ . The method was developed using 102 recordings supervised by an expert and validated with a set of 75 supervised recordings corresponding to different patients, with the proposed method being found to provide consistent results in both quality assessment and the estimation of  $\alpha$ .

The automatic generalized alternating stimulation method has been compared with conventional alternating stimulation (over 2296 registers), masker-probe paradigm (over 158 registers) and triphasic stimulation (over 34 registers). The results show that the proposed generalized alternating stimulation method provides better quality registers than ak, ka, masker-probe paradigm, triphasic or conventional alternating stimulation.

This paper presents an automatic method for applying the proposed generalized alternating method in order to improve the quality of the compound action potentials. Since the automatic quality assessment method is based on

a training set of registers supervised by an expert, its effectiveness relies on expert supervision. However, when the training set is ready, an automatic portable method is available. In addition, the procedure for automatic quality assessment is a useful tool for the development of new methods to reduce stimulus artifact. The use of a criterion based on maximum quality enables the limitations associated with other criteria to be avoided.

Method	set A		set B		set C	
	(N=2296)		(N=158)		(N=34)	
	$\mu_{Q_A}$	$\sigma_{Q_A}$	$\mu_{Q_A}$	$\sigma_{Q_A}$	$\mu_{Q_A}$	$\sigma_{Q_A}$
ak stim.	1.26	1.93	1.51	2.21	2.77	2.76
ka stim.	1.12	1.93	1.49	2.29	2.42	2.85
conv. alt.	2.63	2.80	3.09	3.04	5.28	3.05
mask. probe	-	-	3.69	3.29	-	-
triphasic	-	-	-	-	5.83	3.13
gen. alt.	5.75	2.91	5.87	3.24	7.43	2.26

Table 1

Comparison of different methods of artifact reduction for different sets of registers.

Mean and standard deviation of  $Q_A$  ( $\mu_{Q_A}$  and  $\sigma_{Q_A}$ , respectively) are shown.

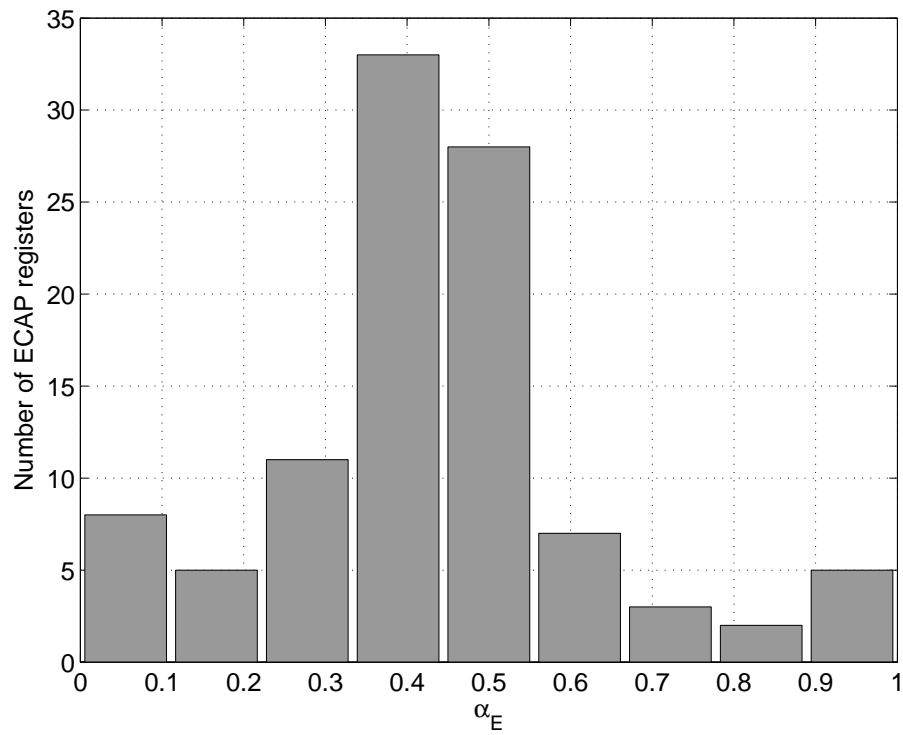


Fig. 1. Distribution of the optimal weight  $\alpha_E$  (proposed by an expert) for the 102 recordings of the supervised database.

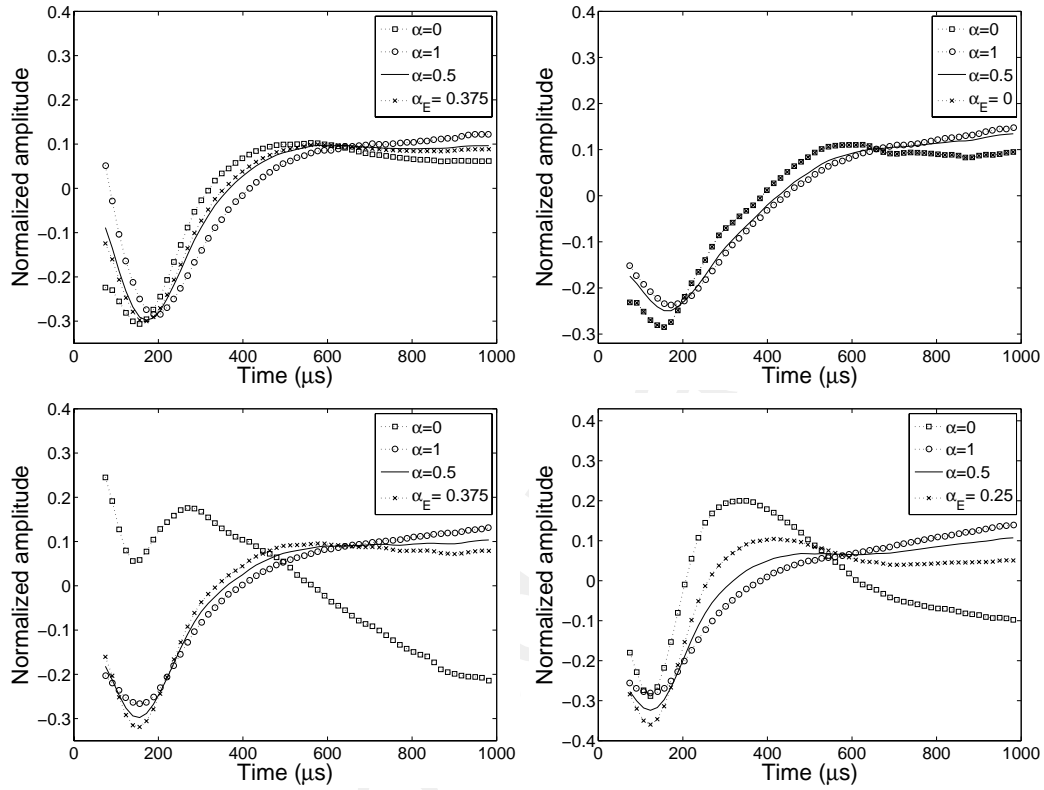


Fig. 2. Four ECAP registers from the supervised database applying the weights  $\alpha = 0$  (ka),  $\alpha = 1$  (ak),  $\alpha = 0.5$  (conventional alternating) and  $\alpha = \alpha_E$  (generalized alternating).

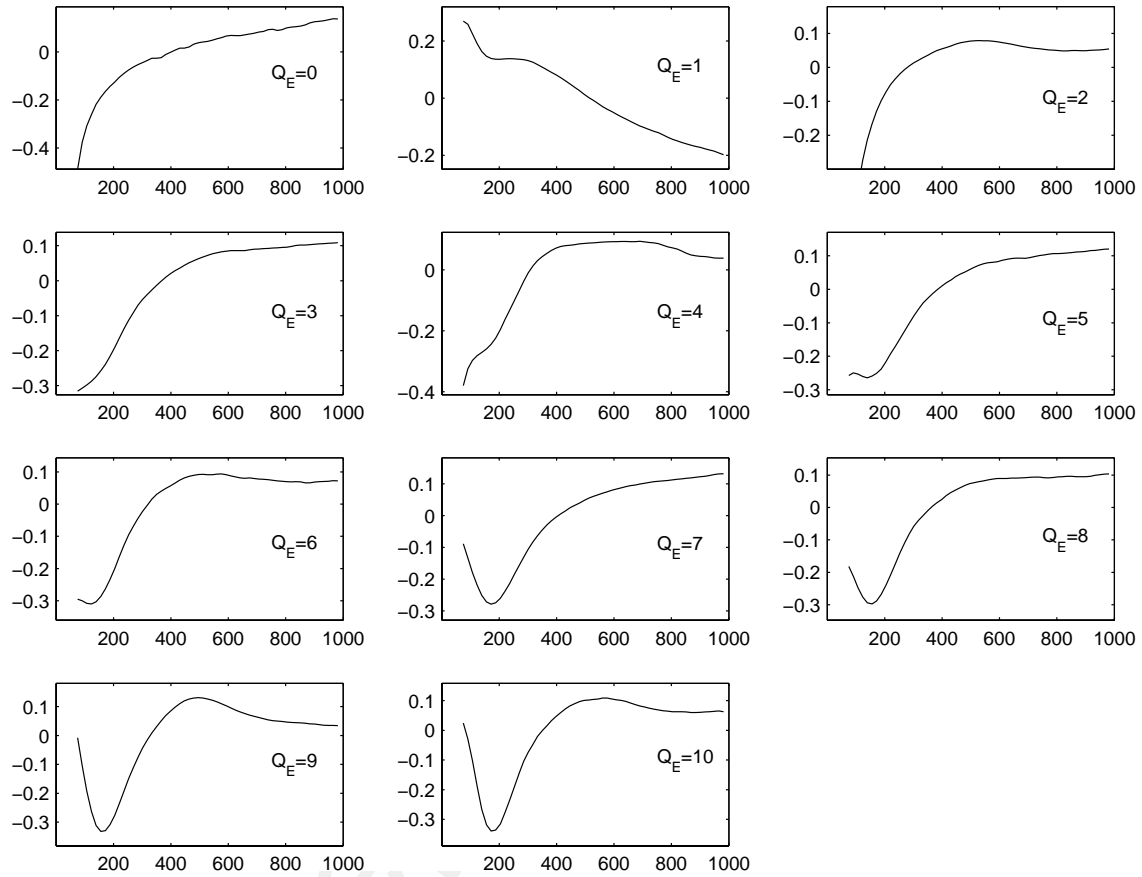


Fig. 3. Instances of ECAP registers (normalized amplitude versus time in  $\mu s$ ) with different quality units assigned by the expert, in the range 0-10.



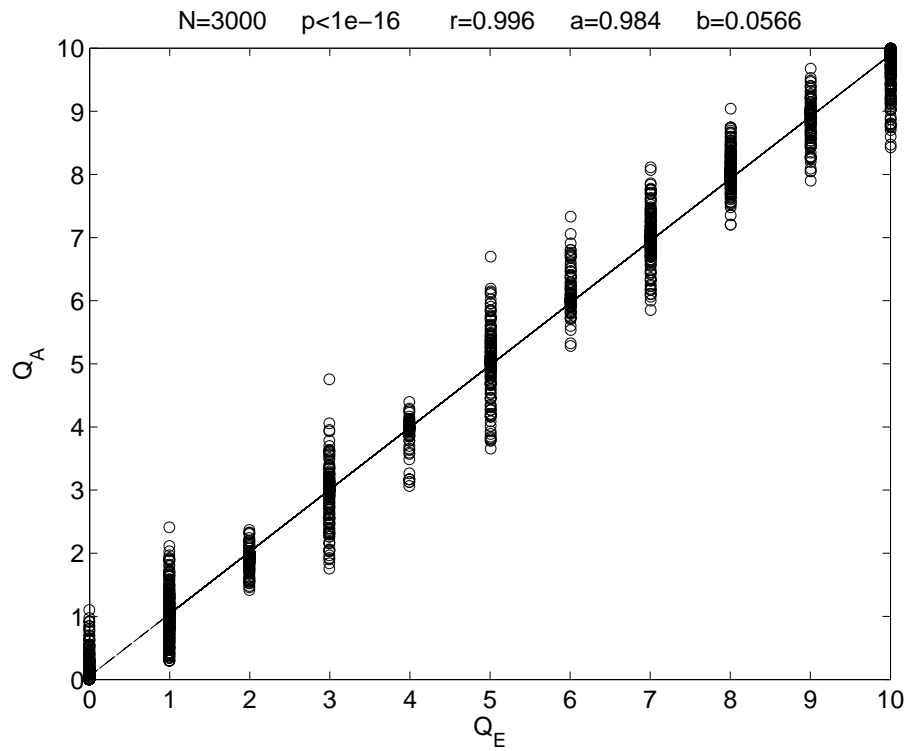


Fig. 4. Linear regression analysis ( $y = ax + b$ ) between the automatic quality ( $Q_A$ ) and the expert quality ( $Q_E$ ) for the 3000 ECAP vectors considered in the estimation of  $Q_A$ . The values of  $p$  (probability associated with the null hypothesis of statistical independence),  $r$  (correlation coefficient),  $a$  and  $b$  (slope and y-intercept of the regression line, respectively) are indicated.

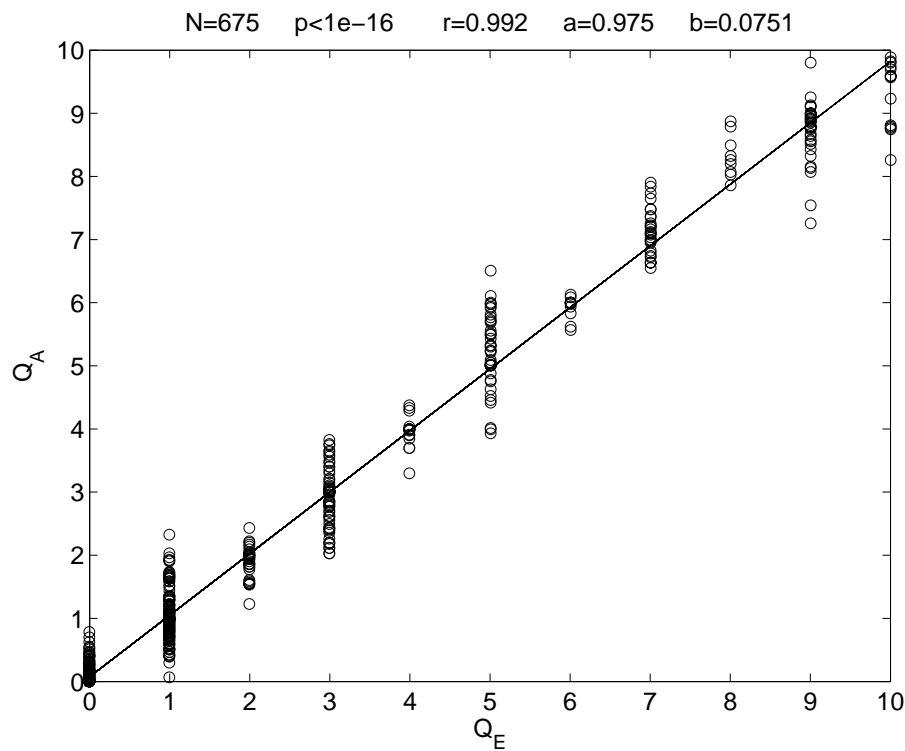


Fig. 5. Linear regression analysis ( $y = ax + b$ ) between the automatic quality ( $Q_A$ ) and expert quality ( $Q_E$ ) for the 675 ECAP vectors considered in the validation set. The values of  $p$  (probability associated with the null hypothesis of statistical independence),  $r$  (correlation coefficient),  $a$  and  $b$  (slope and y-intercept of the regression line, respectively) are indicated.

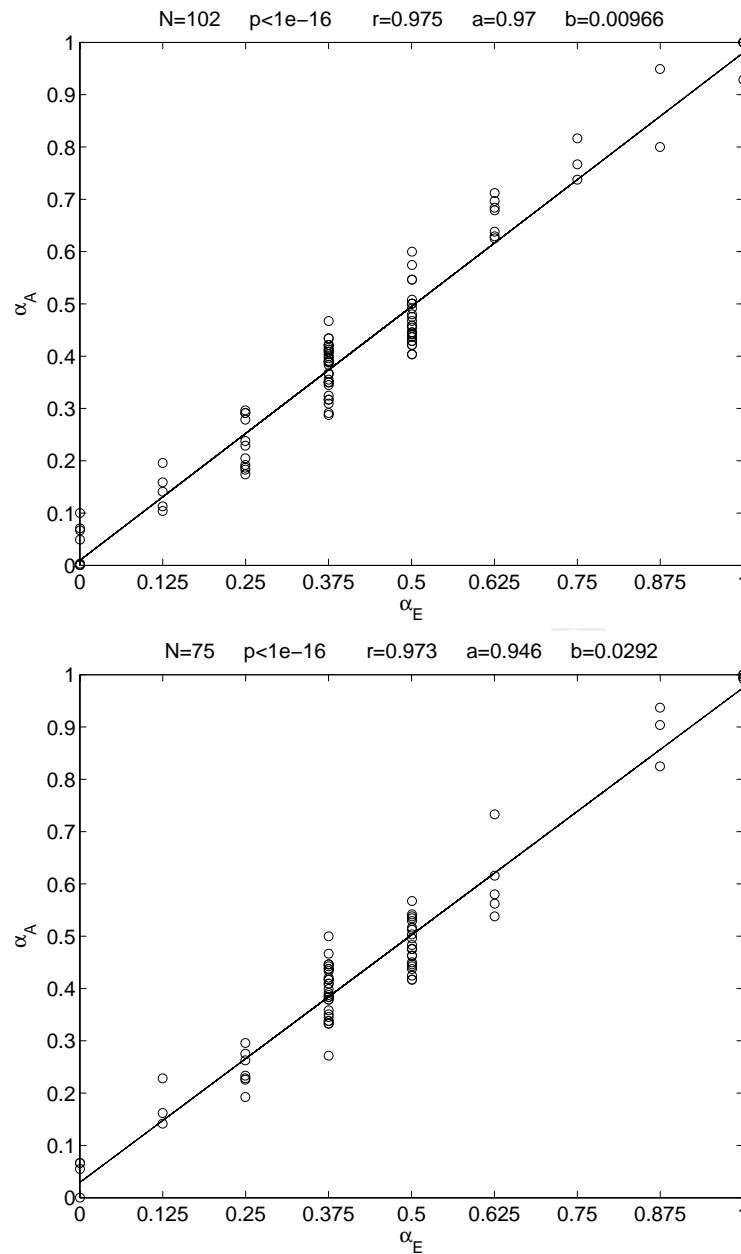


Fig. 6. Linear regression analysis ( $y = ax + b$ ) between the automatic  $\alpha$  ( $\alpha_A$ ) and the estimated  $\alpha$  ( $\alpha_E$ ) for the 102 ECAP recordings included in the training set (up) and for the 75 ECAP recordings included in the validation set (down). The values of  $p$  (probability associated with the null hypothesis of statistical independence),  $r$  (correlation coefficient),  $a$  and  $b$  (slope and y-intercept of the regression line, respectively) are indicated.

## References

- Botros A, van Dijk B, Killian M. AutoNRT: An automated system that measures ECAP thresholds with the Nucleus(R) Freedom cochlear implant via machine intelligence. *Artif Intell Med.*, 2006, In press.
- Brown CJ, Abbas PJ. Electrically evoked whole-nerve action potentials: Data from human cochlear implant users. *The Journal of the Acoustical Society of America*, 1990;88(3):1385-1391.
- Brown CJ, Abbas PJ, Gantz B. Preliminary experience with neural response telemetry in the nucleus CI24M cochlear implant. *The American Journal of Otology*, 1998;19:320-327.
- Dharanipragada S, Visweswariah K. Gaussian Mixture Models with Covariances or Precisions in Shared Multiple Subspaces. *IEEE Transactions on Audio, Speech, and Language Processing*, 2006;14(4):1255-1266.
- Dillier N, Lai WK, Almqvist B, Frohne C. Measurement of the electrically evoked compound action potential via a neural response telemetry system. *The Annals of Otology, Rhinology and Laryngology*, 2002;111(5):407-414.
- Eisen MD, Franck KH. Electrically Evoked Compound Action Potential Amplitude Growth Functions and HiResolution Programming Levels in Pediatric CII Implant Subjects. *Ear & Hearing*, 2004;25(6):528-538.
- Falk TH, Chan WY. Objective Speech Quality Assessment Using Gaussian Mixture Models. *Proc. 32nd Biennial Symposium on Communications*, 2004:169-171.
- Frijns JH, Briaire JJ, de Laat JA, Grote JJ. Initial evaluation of the Clarion CII cochlear implant: speech perception and neural response imaging. *Ear & Hearing*, 2002;23:184-197.
- Frohne C, Brendel M, Behner A. Artefact reduction in Neural Response Imag-

- ing via a modified stimulation signal. 4th International Symposium and Workshops Objectives Measures in Cochlear Implants, Hannover, 2005.
- Geddes LA. Historical evolution of circuit models for the electrode-electrolyte interface. *Annals of Biomedical Engineering*, 1997;25:1-14.
- Gray RM. Oversampled Sigma-Delta Modulation. *IEEE Transactions on Communications*, 1987;35(5):481-489.
- Hedelin P, Skoglund J. Vector Quantization Based on Gaussian Mixture Models. *IEEE Transactions on Speech and Audio Processing*, 2000;8(4):385-401.
- Jackson JE. *A User's Guide to Principal Components*. John Wiley and Sons, 1991.
- Miller CA, Abbas PJ, Rubinstein JT, Robinson BK, Matsuoka AJ, Woodworth G. Electrically evoked compound action potentials of guinea pig and cat: Responses to monopolar, monophasic stimulation. *Hearing Research*, 1998;119:142-154.
- Miller CA, Abbas PJ, Brown CJ. An improved method of reducing stimulus artifact in the electrically evoked whole-nerve potential. *Ear & Hearing*, 2000;21(4):280-290.
- Ragheb T, Geddes LA. Electrical properties of metallic electrodes. *Med. & Biol. Eng. & Comput*, 1990;28:182-186.
- Regan D. *Human Brain Electrophysiology*. New York: Elsevier Science, 1989.
- Sainz M, De la Torre A, Alvarez I, Spitzer P. Processing of artifact in electrically evoked action potentials. 4th International Symposium and Workshops Objectives Measures in Cochlear Implants, Hannover, 2005.
- Schoesser H, Zierhofer C, Hochmair ES. Measuring electrically evoked compound action potentials using triphasic pulses for the reduction of the residual stimulation artifact. *Conference on Implantable Auditory Protheses*, Asilomar, 2001.

Schoesser H, Nobbe A, Brill S, Spitzer P, Zierhofer C. Influence of stimulation pulse shape on nerve excitation threshold: investigations using a state-space model and preliminary results PulsarCI100 users. Conference on Implantable Auditory Protheses, Asilomar, 2005.

Zhuang X, Huang Y, Palaniappan K, Zhao Y. Gaussian mixture density modeling, decomposition, and applications. IEEE Transactions on Image Processing, 1996;5:1293-1320.

Zierhofer C. Adaptive Sigma-Delta Modulation with One-Bit Quantization. IEEE Transactions on Circuits and Systems, 2000;47(5):408-415.