

Detecting Neural Responses in EEG Recordings of Cochlear-Implant Recipients

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Preface

I was introduced to cochlear implants through a discussion with employees of Cochlear Ltd. on VTK's job fair. Ever since, I have been fascinated by these devices and their ability to restore hearing. Throughout the past year, I had the opportunity to work on a topic concerning cochlear implants. I am grateful to everyone who has been involved in this thesis.

I would like to thank my mentor, Julian, for guiding me through the process of conducting research and writing this thesis. Our discussions deepened my understanding of the topic and helped to unfold the narrative as presented in this thesis. Your feedback on initial versions has improved this text significantly. Thank you for inviting me to the lab during the acquisition of EEG recordings from a cochlear implant recipient. His experiences with a cochlear implant showed me the impact the research on these devices has in practice.

I would also like to express my gratitude to my supervisors, prof. dr. ir. M. Moonen and prof. dr. J. Wouters, for providing me with the possibility to explore this fascinating topic; and to my assessors, prof. dr. ir. A. Bertrand and ir. W. David., for reading and assessing this thesis dissertation.

Lastly, I would like to thank my family for supporting me in the process of writing this thesis; special thanks go to both my friend Jonas and my uncle for proofreading this text.

Dear reader, I appreciate your time and interest to read this thesis, and hope it inspires the same fascination in you as it has in me.

Tom Colemont

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Abstract

Cochlear implants (CIs) restore hearing in individuals suffering from severe sensorineural hearing loss. In recent years, electrically evoked auditory steady-state responses (EASSRs) have been studied to automate the calibration of the CI's stimulation settings to optimize its performance. EASSRs are evoked through an amplitude-modulated high-rate pulse train and can be objectively detected in EEG recordings at the modulation frequency using statistical tests. However, electrical stimulation artifacts of the CI hinder the detection of EASSRs in CI recipients.

This thesis dissertation has two research objectives. First, it aims to characterize the stimulation artifact and to determine the effects of nonidealities and nonlinearities on this artifact. Second, it explores how the knowledge of the artifact characteristics and the effects of nonidealities and nonlinearities can be leveraged to develop artifact suppression methods.

In the context of the first research objective, an analytical expression for the spectrum of the stimulation signal is derived. A more accurate signal representation is proposed which takes the practical constraints of the pulse generation into account. It shows that the stimulation signal inherently contains an artifactual component at the modulation frequency. The effects of nonidealities and nonlinearities are found to further magnify this component. An experimental set-up including a head phantom is used to characterize the stimulation artifact in practice. Its results are in accordance with the theoretical analysis.

Regarding the second objective, three methods are developed in the context of this thesis. These are evaluated on a test set containing EEG recordings of 10 CI recipients, using MP mode stimulation and a pulse rate of 900 pulses per second. A first method exploits the differences in temporal characteristics of the EASSR and artifact, and can be interpreted as an alternative implementation of the existing Kalman filter-based methods. It is effective in contralateral channels but fails to detect EASSRs in ipsilateral channels. A second method is a novel approach and exploits the different effects of the pulse averaging operation on the stimulation artifact and the EASSR to attenuate the former. It is effective in contra- and most ipsilateral channels. The last method extends the recently introduced linear system identification by including nonlinearities in the artifact model. The absence of ground truth EASSR characteristics complicates its evaluation. However, the performance of this method appears slightly improved in comparison to the linear model.

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List of Abbreviations and Symbols

Abbreviations

AEP	Auditory evoked potential
AM	Amplitude modulation
ASSR	Auditory steady-state response
BP	Bipolar mode stimulation
CI	Cochlear implant
CI-IB	Cochlear implant in a box
CL	Current level
C-level	Comfortable level
CPA	Conditioned play audiometry
EASSR	Electrically evoked auditory steady-state response
EEG	Electroencephalography
ICA	Independent component analysis
IPI	Interpulse interval
LI	Linear interpolation
LSI	Linear system identification
MaL	Left mastoid electrode position
MaR	Right mastoid electrode position
MEG	Magnetoencephalography
MLE	Maximum likelihood estimator
MP	Monopolar mode stimulation
NLI	Nonlinear system identification
OLS	Ordinary least squares
PA	Pulse asymmetry; Pulse averaging
pps	Pulses per second
RF	Radio frequency
RMS	Root mean square
SI	System identification
TDAS	Time domain artifact suppression
T-level	Threshold level
TS	Template subtraction
VRA	Visual reinforcement audiometry

Symbols

Chapter 2: Preliminaries

I_A	Stimulation current expressed in amperes
I_{CL}	Stimulation current expressed in current levels

Chapter 3: Theoretical Artifact Analysis

$\Pi(\frac{t}{T})$	Rectangular box function of duration T
t	Time
f	Frequency
ω	Radial frequency
θ	Phase in radians
j	Imaginary unit
$\delta(t)$	Dirac delta function
$s(t)$	Normalized carrier signal
$p(t)$	Biphasic, cathodic-first pulse
$f(t)$	Stimulation pulse train
$m(t)$	Modulating signal
$g(t)$	Stimulation signal
$g_{ideal}(t)$	Ideal stimulation signal
$g_{pract}(t)$	Practical stimulation signal
$P(f)$	Fourier transform of biphasic, cathodic-first pulse
$P_{sym}(f)$	$P(f)$ in case of symmetry
$F(f)$	Fourier transform of stimulation pulse train
$M(f)$	Fourier transform of modulation signal
$G_{ideal}(f)$	Fourier transform of ideal stimulation signal
$G_{pract}(f)$	Fourier transform of practical stimulation signal
A_p	Amplitude of the positive pulse
A_n	Amplitude of the negative pulse
A	Amplitude of the symmetrical pulse
T_p	Duration of the positive pulse
T_n	Duration of the negative pulse
T_i	Duration of the interphase gap
T	Duration of the symmetrical pulse
A_m	Modulation amplitude
D	Modulation depth
ϕ_m	Modulation phase
f_m	Modulation frequency
f_c	Carrier frequency
T_c	Carrier period

Chapter 4: Experimental Artifact Analysis

$PA(p)$	Pulse asymmetry measure
$x(t, p)$	p -th pulse of the measured EEG-signal
f_{m1}	Lowest modulation frequency
f_{m2}	Highest modulation frequency
$h(\cdot)$	Fitted surface
x	Distance to the stimulation electrode in centimeters
y	Stimulation level in amperes
A	Exponential amplitude parameter
B	Exponential decay parameter
C	Linear slope parameter
D	Intercept parameter

Chapter 5: Artifact Suppression Methods

L	Latency expressed in seconds
a	Linear slope expressed in degrees per Hz
N	Number of samples in an interpulse interval
K	Number of samples of the mean epoch EEG-signal
z^{f_m}	Mean epoch at f_m
r^{f_m}	Estimated response at f_m
a^{f_m}	Estimated artifact at f_m
c^{f_m}	Cosine oscillating at f_m
s^{f_m}	Sinusoid oscillating at f_m
u^{f_m}	Artifact input signal at f_m
$s_{est}^{f_m}$	Sum of estimated response and artifact at f_m
m	Skipping mask
R^{f_m}	Response regression matrix at f_m
C^{f_m}	Response filter matrix at f_m
U^{f_m}	Artifact filter matrix at f_m
$U_n^{f_m}$	Artifact filter matrix at f_m of order n
$\mathbf{b}_{resp}$	FIR-coefficients of response model
$\mathbf{B}_{resp}$	Frequency domain representation of $\mathbf{b}_{resp}$
$\mathbf{b}_{arti}$	FIR-coefficients of artifact model
$\mathbf{b}_{artin,n}$	Coefficients of artifact model of n -th order nonlinearities
q	Shift factor expressed in samples
N_1	Response FIR-filter order
N_2	Artifact FIR-filter order
$\mathbf{z}$	Column vector of the concatenated mean EEG-epochs
$\mathbf{H}$	Signal model regression matrix
$\mathbf{x}$	Vector of unknown FIR-coefficients

LIST OF ABBREVIATIONS AND SYMBOLS

$\mathbf{v}$	Noise vector
J^{f_m}	Least-squares cost function at f_m
J	Total least-squares cost
$A_{EASSR}^{f_m}$	Estimated EASSR amplitude at f_m
$\theta_{EASSR}^{f_m}$	Estimated EASSR phase at f_m
$\mathbf{a}_{exp}$	Exponentially decaying signal in an interpulse interval
$\mathbf{a}_{bias}$	Bias signal in an interpulse interval
A_{exp}	Block diagonal matrix of matrix of $\mathbf{a}_{exp}$
A_{bias}	Block diagonal matrix of matrix of $\mathbf{a}_{bias}$
α	Decay factor of exp. decaying template; reg. hyperparameter
β	Regularization hyperparameter
γ	Regularization hyperparameter
λ	Regularization hyperparameter
Γ	Tikhinov regularization matrix
$v(p)$	Signal of pulse averages
$\delta_{i,...,k}$	Kronecker Delta function

Chapter 1

Introduction

1.1 Context

According to the World Health Organization (WHO), more than 430 million individuals require intervention to address their disabling hearing loss. By 2050, this number is projected to exceed 700 million. [48] Among these are deaf and severely hearing-impaired individuals, for whom the acoustic amplification provided by traditional hearing aids is no longer sufficient to restore their sound perception. For them, cochlear implants (CIs) may offer a solution through a direct and electrical stimulation of the auditory nerve. In this manner, a CI is able to bypass the deficient transducer structures in their auditory system. [50] The number of CI recipients is growing exponentially, with over one million individuals having received a CI as of July 2022. [18, 37]

Since Volta’s discovery that electricity can evoke auditory sensations more than 200 years ago, CIs have achieved significant technological advancements and are now considered among the most successful medical prostheses. [44, 47, 51] However, in order to obtain adequate speech understanding and enhance the listening experience, the stimulation settings of the CI have to be calibrated depending on the particular needs of the recipient. Such a calibration process, known as fitting, involves determining the hearing threshold (T-level) and comfortable (C-level) stimulation levels for each stimulation electrode of the CI. Despite its importance, the fitting process is currently facing several challenges. [14, 40]

The first and most stringent is its reliance on behavioral feedback, which is impractical for infants, children, and populations unable to provide such feedback. Secondly, the fitting process is time-consuming and requires the expertise of a trained audiologist, which results in a high clinical burden and associated costs. Thirdly, the obtained stimulation settings are not objective as they may depend on the experience or preference of the audiologist, complicating the comparison of fitting outcomes across recipients. [14, 40] Lastly, the fitting sessions only take place during occasional visits to the audiologist and thus cannot continuously adapt to time-varying factors such as different listening environments or progression in hearing loss. [44]

These challenges have been addressed in several ways. First, to cope with the lack of behavioral feedback, methods such as visual reinforcement audiometry (VRA) and conditioned play audiometry (CPA) aim to teach individuals to perform a task when they perceive a sound to determine the T-levels. [14, 46] Second, to reduce the fitting time and costs, the T- and C-levels of only a subset of the electrodes can be determined. As these levels show limited variation across electrodes in certain stimulation modes, the levels of the remaining electrodes can be approximated by interpolating between the determined values. [14, 42, 51]

Since these proposals do not address all challenges, research in the field of CI fitting has in recent years shown interest in neural responses as objective measures. These neural responses can be objectively detected without any form of feedback through electroencephalography (EEG), which records the neural activity of the brain. A specific type of neural response, the auditory steady-state response (ASSR), shows promising results to determine hearing thresholds in normal hearing subjects, and may thus be used for objective fitting. In CI recipients, this neural response is referred to as an electrically evoked auditory steady-state response (EASSR) due to the CI's electrical stimulation of the auditory nerve required to elicit them. [38, 40]

1.2 Problem Statement

In normal hearing subjects, ASSRs can be objectively determined in the frequency domain representation of the EEG recordings using statistical tests. [14, 38] In CI recipients on the contrary, these recordings are contaminated with artifacts originating from the electrical stimulation of the CI itself. As these artifacts overlap in both the time and frequency domain with the elicited EASSR, there is a significant risk for a false positive EASSR detection when no artifact suppression algorithms are applied to the EEG recordings prior to the analysis. [40]

Next to CI fitting, the stimulation artifacts also complicate the study of the electrode-neuron interface, and research on the auditory plasticity and maturation in CI recipients. [14] The problem of electrical stimulation artifacts of EEG recordings also arises in other fields, such as somatosensory stimulation, transcranial magnetic and current stimulation, and deep brain stimulation. [16]

1.3 Thesis Objectives

This thesis is concerned with the detection of EASSRs in EEG recordings of CI recipients. Outside of the introduction and preliminaries, this thesis is divided into two main parts.

Part 1: Characterization of the Stimulation Artifact

The first part aims to characterize the stimulation artifacts in the EEG recordings and identify the potential nonidealities and nonlinearities causing and/or contributing to these artifacts. Although literature often mentions that these artifacts likely originate

from nonidealities and nonlinearities [22, 27, 40], their nature and contribution to the stimulation artifact is still not fully understood. Previous research on artifact characterization has primarily focused on amplitude, duration, and morphology [16] as well as the effect of different stimulation settings [32]. The first part of this thesis focuses on a theoretical and experimental characterization of the nonlinearities and nonidealities of the artifact in the context of EASSR detection. Such a characterization is relevant as it can guide the development of more accurate artifact suppression methods.

Part 2: Development of Artifact Suppression Methods

The second part aims to develop methods to suppress the stimulation artifacts, enabling the detection of EASSRs in EEG recordings of CI recipients. It explores whether the knowledge gained from the first part can be leveraged to develop more accurate EASSR detection methods. Additionally, it studies whether incorporating nonidealities and nonlinearities into existing EASSR detection methods is able to enhance their performance. The performance of these methods is evaluated on EEG recordings of CI recipients, obtained at a stimulation level below the hearing threshold and at a comfortable stimulation level. In this manner, it can be evaluated whether the methods can detect the presence of an EASSR and its characteristics.

Research Questions

The objectives which the first and second parts aim to achieve can be reformulated into two main research questions:

1. Which nonidealities and nonlinearities cause and/or contribute to the stimulation artifact, and what are their defining characteristics?
2. How can the knowledge of these nonidealities and nonlinearities be leveraged in the development of and extensions to methods which aim to separate the stimulation artifact and EASSR?

1.4 Outline of the Thesis

This section provides an outline of the thesis and briefly summarizes the contents of each chapter.

Chapter 2: Preliminaries

This chapter provides the preliminaries and background information required for the subsequent chapters of this thesis dissertation. An overview of a CI is provided, along with the characteristics of electroencephalography (EEG), which is used to record the neural responses. It further discusses the characteristics of these responses and the electrical artifact. Finally, existing artifact suppression methods are reviewed.

Chapter 3: Theoretical Artifact Analysis

This chapter presents a theoretical analysis of the stimulation artifact by deriving the time and frequency domain representations of the ideal stimulation signal analytically. A signal representation which takes the practical limitations of the pulse generation

process into account is proposed as a more accurate description of the stimulation signal and artifact. Additionally, the effects of nonidealities and nonlinearities on the stimulation artifact are studied in the context of the first research question. This analysis results in three theoretical statements about the stimulation artifact.

Chapter 4: Experimental Artifact Analysis

To validate these theoretical statements in practice, a dataset of EEG recordings containing only stimulation artifacts is collected. These recordings are obtained using an experimental set-up with a head phantom to mimic the artifact propagation through the human head. These analyses result in an experimental characterization of the stimulation artifact, and a quantification of the studied nonidealities and nonlinearities.

Chapter 5: Artifact Suppression Methods

Based on the theoretical and experimental analyses, three EASSR detection methods are presented. The first method can be interpreted as an alternative implementation of the Kalman filter method introduced in [34] and further extended in [14]. The second method exploits the different effects of a pulse averaging operation on the stimulation artifact and the EASSR to attenuate the former. The last method extends the linear system identification introduced in [40] by including nonlinearities in the artifact model. The first method is related to the existing Kalman filter-based methods, while the last method is a direct extension to an existing method. The second method is a novel approach.

Chapter 6: Results

This chapter presents the EASSR detection accuracy of the developed methods and compares it to a baseline which does not apply any form of artifact suppression. The performance of each method is evaluated on its false positive rate, its detection accuracy, and the estimated EASSR characteristics.

Chapter 7: Discussion

This chapter discusses the results shown in the previous chapter, with a focus on the artifact suppression quality and the estimated EASSR characteristics. The differences and similarities between the methods and their performance are highlighted and interpreted.

Chapter 8: Conclusion and Future Work

This chapter concludes this thesis dissertation by reflecting upon the two research questions and offers suggestions for future work.

Chapter 2

Preliminaries

2.1 Introduction

This chapter provides the preliminaries and background information required for the work presented in this thesis dissertation. [Section 2.2](#) introduces the working principles and components of a cochlear implant (CI). Then, [Section 2.3](#) discusses the characteristics of, and acquisition and preprocessing steps applied to the EEG-signals which record both the EASSR and the stimulation artifact. Next, [Section 2.4](#) and [Section 2.5](#) discuss the characteristics of the (E)ASSRs and stimulation artifacts respectively. Subsequently, [Section 2.6](#) provides an overview on existing artifact suppression methods. Finally, [Section 2.7](#) concludes the chapter.

2.2 Cochlear Implants

Individuals with sensorineural hearing loss may experience severe to profound hearing impairment, for which the frequency-specific acoustic amplification provided by traditional hearing aids is no longer sufficient. For these individuals, cochlear implants (CIs) are used to restore hearing through a direct electrical stimulation of the auditory nerve, thereby circumventing the malfunctioning transducer structures in their auditory system. [\[40, 50\]](#)

A CI comprises both external and internal components. The external part includes a microphone, a sound processor, and a radio frequency (RF) coil. The internal part consists of an internal RF coil, and the implant itself. The latter contains a casing electrode, a ball electrode, and an electrode array which is inserted into the cochlea. [\[14, 40\]](#) Depending on the device and manufacturer, the electrode array contains 12 to 22 intracochlear and one or two extracochlear electrodes. [\[15, 50\]](#) [Figure 2.1](#) illustrates the components of a CI.

The working principle of a CI can be summarized as follows. The external microphone captures an audio signal, which is further preprocessed and converted into an electrical stimulation sequence by the external sound processor. The conversion from the preprocessed audio signal to the stimulation sequence depends on the applied

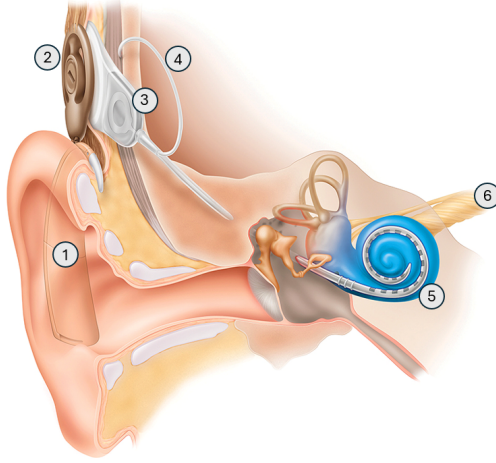


FIGURE 2.1: A cochlear implant device consists of a microphone and sound processor (1), an internal and external RF coil (2), the implant itself and the casing electrode (3), the ball electrode (4), and the electrode array (5). (6) shows the auditory nerve, which is electrically stimulated by the implant. This figure from [12] has been adapted with added numbering. The labeling of the components is based on [14, 26].

stimulation strategy, and typically involves band-pass filtering and envelope extraction. A detailed discussion on and an extensive overview of stimulation strategies are available in [50]. The electrical stimulation sequences are then transmitted to the internal piece of the implant through communication between the external and internal RF coil. Next, the internal piece of the implant decodes the received stimulation sequences and generates the stimulation pulses. These are applied to the intracochlear stimulation electrode(s) of the electrode array, which is inserted into the cochlea and allows for a direct, electrical stimulation of the auditory nerve. In this manner, the defective structures in the middle and inner ear are bypassed. [14, 50, 40] Besides facilitating communication between the external and internal components, the RF coils are also used to power the internal components of the implant through electromagnetic induction. [44] Figure 2.2 provides a high-level overview of the working principle of the CI system.



FIGURE 2.2: A high-level overview of the working principles of the CI system. This figure is recreated based on [50].

In order to apply the electrical stimulation signal, both an active and reference stimulation electrode are selected. The active electrode is part of the electrode array and defined by the stimulation strategy. The reference electrode can be either an intra- or extracochlear electrode. Stimulation between two intracochlear electrode is referred to as bipolar (BP) mode stimulation, whereas monopolar (MP)

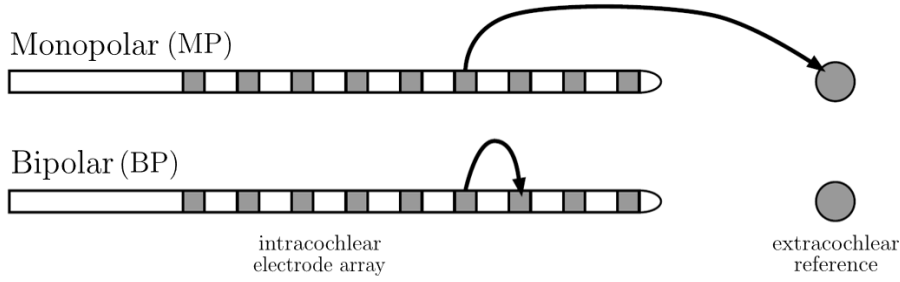


FIGURE 2.3: An illustration of monopolar and bipolar mode stimulation. This figure has been adapted from [44].

mode stimulation refers to stimulation between one or more extracochlear and an intracochlear electrode. The increased physical separation between the reference and active stimulation electrodes in the MP mode stimulation results in a wider stimulation. This is associated with lower threshold stimulation levels (T-levels) and less variation between these T-levels. The lower stimulation levels in this mode result in a prolonged battery life. These properties make MP mode stimulation preferred in clinical practice. [14, 42] Figure 2.3 illustrates both stimulation modes.

In this thesis dissertation, devices of Cochlear Ltd. are used. Other manufacturers in the market include Med-El, Advanced Bionics, Nurotron, and Oticon Medical. Although the fundamental operational concepts are similar across all manufacturers, stimulation strategies and hardware may be different among them. [44]

As previously mentioned, the performance of CIs heavily depends on the stimulation parameters determined during a fitting process. [40] Such a fitting process results in an ensemble of patient-specific stimulation parameters - often referred to as a map - which yields the optimal performance for the CI recipient. [50] Despite its importance, the fitting process is hindered by the need for behavioural feedback, the time requirements and associated costs, the lack of objectivity in the determination of the map and the infrequent adaptation of these stimulation parameters. Especially the first factor is problematic in hearing-impaired infants and children, which form an important target demographic of CIs as their early implantation leads to better speech and language development. [5, 14]

2.3 Electroencephalography

In order to address these issues, objective neural measures are being studied to automate the fitting process. These neural measures are often recorded in an electroencephalogram. Although both magnetoencephalography (MEG) and electroencephalography (EEG) have a sufficiently high temporal resolution to detect these neural measures, MEG is not recommended for CI recipients due to the magnetic fields. Consequently, EEG is favored and used to record these neural measures. [14] This section will consider the characteristics, drawbacks, and benefits of EEG. Next, the acquisition of EEG recordings is discussed, after which the preprocessing procedures are considered.

2.3.1 Characteristics

EEG is a non-invasive method to record the electrical activity in the brain. This activity is generated by the synchronous firing of large populations of neurons in the brain, resulting in measurable voltage differences. These signals can be recorded by electrodes which are placed non-invasively on the scalp of the subject. A minimization of the impedance of the electrode-scalp interface is required to optimize the signal quality. Therefore, a gel is typically applied to reduce this impedance. Dry EEG systems do however exist as well, with comparable performance for brain-computer interface and auditory applications. [23, 44]

EEG has a number of benefits. First of all, it is a non-invasive method. Additionally, it requires less expensive and less complex equipment as compared to MEG. [44] Finally, the high temporal resolution of EEG allows to record the neural measures required to automate the CI fitting process. [14]

However, EEG also has a number of drawbacks. First, the application of the EEG electrodes and the gel is time-consuming. A second disadvantage is the low spatial resolution of EEG which directly leads to a low signal-to-noise ratio (SNR) of the raw EEG recordings, since the signal of interest is only measurable alongside the total brain activity. The last drawback is its susceptibility to artifacts, which are either biological or technological in nature. Eye-blink and muscle artifacts are examples in the former class and will be removed in the preprocessing procedure as explained in the next subsection. The latter class contains the stimulation artifacts, of which the suppression is the topic of this thesis. [10, 44]

2.3.2 Acquisition and Preprocessing of EEG recordings

In order to cope with the low SNR of EEG and its susceptibility to artifacts, the EEG recordings are preprocessed prior to the analysis. [44] This subsection discusses both the acquisition and preprocessing procedures of the EEG recordings in detail.

The EEG acquisition and preprocessing procedures are taken from [40] and summarized in this text. The dataset of real subject data, available prior to the start of this thesis and described in Section 5.2, is acquired and preprocessed according to the description below. The dataset of stimulation artifact, acquired in the context of this thesis and described in Subsection 4.2.2, follows the description below as well. Using the same EEG equipment and preprocessing procedures in all datasets ensures that these aspects do not introduce any bias. [10]

The EEG recordings are acquired using a Biosemi ActiveTwo Hyper-Rate EEG recording system with a sampling rate of 262144 Hz. EEG is recorded at eight electrodes, six of which are placed at *P9*, *P10*, *Iz*, *Cz*, *Fz*, and *Fpz* as defined in the international 10-20 system, shown in Figure 2.4. Two additional electrodes are located at the left and right mastoid, referred to as *MaL* and *MaR* respectively. When the CI coil was located at an electrode position, the closest electrode position was used.

For each EEG recording, 300 epochs with a duration of 1.024 seconds each are recorded in an electromagnetically shielded room. All frequencies involved in the stimulation signals are rounded to avoid spectral leakage. The recorded EEG is low-pass filtered using a third-order anti-aliasing filter which is built into the system. This filter has its -3 dB point at 50 kHz. All processing is done offline using MATLAB R2022b. The data is referenced offline to one of the reference electrodes. The EEG recordings are detrended with a second-order polynomial to remove drifts over a window of half a second. Using the triggers of the stimulation, the recordings are split into epochs of 1.024 seconds each. Five percent of the epochs are rejected based on peak-to-peak amplitudes. The epoch rejection based on this criterion removes the biological artifacts; such an approach is possible due to the short duration of a single epoch. Furthermore, it is free of user bias and allows to use the same preprocessing pipeline for all EEG recordings. All non-rejected epochs are averaged to attenuate the noise, resulting in the mean EEG epoch used in the analysis. [40]

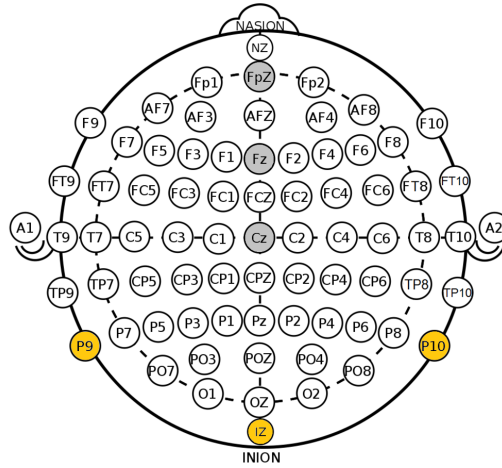


FIGURE 2.4: The EEG electrode positions as defined by the international 10-20 system. The selected reference and analysis electrodes are indicated in gray and yellow electrodes respectively. *MaL* and *MaR* are not indicated. Figure is obtained from [11], changes are limited to colouring the relevant electrodes

2.4 Auditory Steady State Responses

So far, the objective neural measure to be detected has only been loosely defined. Any objective neural measure which correlates well with behaviourally determined T- and C-levels shows the potential to automate the fitting process. In this context, the objective neural measure is an auditory evoked potential (AEP), which is an electrical response generated after stimulation of the auditory system. In normal-hearing subjects, this response is evoked by acoustic stimulation, whereas electrical stimulation is required in CI recipients. [44] The search for an AEP capable of automating the fitting process is a research field in itself, and falls outside the scope of this thesis. An overview of AEPs and their potential to automate the fitting

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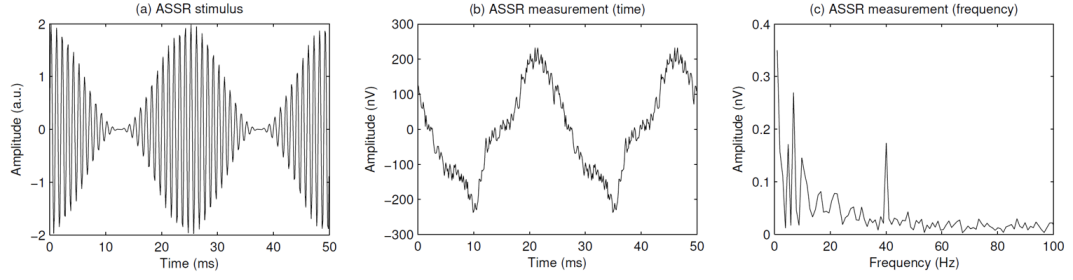


FIGURE 2.5: (a) The acoustic stimulus, a modulated sinusoid, to evoke an ASSR at the modulation frequency. (b) Time domain: two periods of an ASSR after averaging. (c) Frequency domain: spectrum of the mean epoch, displaying a peak at the modulation frequency. Figures are taken from [14]

process is available in [14, 44].

This thesis will focus on the detection of electrically evoked auditory steady-state responses (EASSRs) for two reasons. First, in normal-hearing subjects, this AEP has demonstrated the possibility to determine hearing thresholds, indicating it is a promising tool to automate the fitting procedure. [38, 40] Secondly, this thesis dissertation continues upon the research conducted in the recently introduced system identification method by J. Schott *et al.* [40] and the doctoral dissertation of H. Deprez [14]; both of which focus on the detection of EASSRs.

(E)ASSRs are neural auditory steady-state responses, which result from the neural phase-locking to periodic stimulation signals, which amplitude modulate a carrier signal. [14, 40] A main benefit of EASSRs is their objective detectability in an electroencephalogram. In the frequency domain, an (E)ASSR presents itself as a distinct spectral peak at the modulation frequency of the stimulation signal which can be automatically detected using statistical tests. This automatic detection differentiates them from transient responses, which typically involve a manual labeling of the response peaks. [14, 38] Figure 2.5 illustrates the stimulation signals, and the ASSR in both the time and frequency domain.

In CI recipients, EASSRs are evoked by electrical stimulation. Cochlear Ltd. uses symmetric, biphasic, cathodic-first pulses as the carrier signal, [14] which is further discussed and analyzed in Section 2.5 and Chapter 3. Except for the different carrier signals in the stimulation, the evocation of an EASSR is conceptually identical to ASSRs shown in Figure 2.5.

A basic knowledge of the characteristics of (E)ASSRs is required for the development of (E)ASSR detection algorithms. The stimulation signal $g(t)$, either acoustic or electrical, can be represented as:

$$g(t) = s(t) \cdot A_m \cdot (1 + D \cdot \cos(2\pi f_m t + \phi_m)) \quad (2.1)$$

in which $s(t)$ represent the normalized carrier signal; A_m , D , f_m , and ϕ_m the modulation amplitude, depth, frequency, and phase respectively. [40]

In normal-hearing subjects, ASSRs can be evoked by modulation frequencies f_m between 1 Hz and 200 Hz but are particularly pronounced in the frequency range around 40 Hz. [38] As processing in the brain requires time, there is a delay between the generation of an (E)ASSR and the stimulation. This delay, further referred to as latency, is about 40 ms. [38, 21] An increased stimulus intensity A_m results in increased response amplitudes and decreased response latencies. As the modulation depth D increases, the response amplitude increases as well since the brain predominantly focuses on the auditory envelope. An increase of the frequency f_c of the carrier signal $s(t)$ results in a significant decrease in amplitude of the 40 Hz ASSR, and a decreased latency. [38] The fact that EASSRs can be evoked using clinically relevant carrier frequencies of 900 Hz is especially beneficial in the perspective of automating the fitting process, as T- and C-levels show a dependency on the stimulation rate. [14, 35] Note that the carrier frequency must be at least a factor four larger than the modulation frequency for an accurate detection of the EASSR. [14] Lastly, (E)ASSRs are able to exhibit nonlinear characteristics, resulting in spectral peaks at harmonics of the modulation frequency f_m . [22, 38]

2.5 Cochlear Implant Artifacts

The most substantial obstacle in reliably detecting EASSRs in CI recipients is the contamination of electrical artifacts in their EEG recordings which originate from the CI device itself and are thus inevitable. These artifacts overlap with the EASSR in both the time and frequency domain, which results in a risk of false positive EASSR detections. [14, 40] This section describes the characteristics of this artifact and its dependence on the stimulation settings.

The two main contributions to electrical artifacts originate from the radio frequency link between the RF coils and the stimulation pulse sequences which are applied to the electrodes. Both of these artifacts overlap with the EASSR in the time domain. Since the frequencies used for RF communication are in the MHz range and the stimuli are nonlinearly encoded, the RF contribution to the electrical artifact typically does not overlap with the EASSR in the frequency domain. The contribution of the stimulation signal to the electrical artifact - referred to as the stimulation artifact in the remainder of this text - is however able to contain a spectral component at the modulation frequency, resulting in a spectral overlap with the EASSR. [40, 51, 14]

Figure 2.6 illustrates the applied stimulation signal in the first subfigure. As its stimulation level is below the hearing threshold, no EASSR is evoked. The EEG recording thus contains solely the stimulation artifact and is depicted in the time domain in the second subfigure. Note that the stimulation pulses can be recognized directly in the EEG recording. The amplitude of these pulses in the EEG recording is typically multiple orders of magnitude larger than the EASSR. [44]. Next, the third subfigure shows the electrical artifact in the interpulse interval (IPI), which is the time interval between two subsequent pulses. In this interval, the electrical artifact is characterized by a clear undershoot followed by an exponentially decaying

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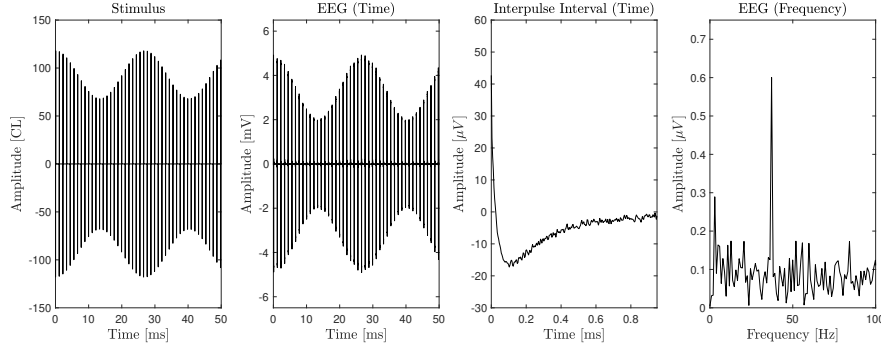


FIGURE 2.6: The stimulation signal expressed in current levels (see *infra*) (left), an ipsilateral (see *infra*) EEG recording obtained at a subthreshold stimulation level in the time-domain (second from the left), a zoom of the interpulse interval of this EEG recording (second from the right) and the frequency domain representation of this EEG recording (right).

tail. The latter is assumed to originate both from the anti-aliasing low-pass filter and the capacitive effects of the electrode-tissue and skin-gel-EEG electrode interface. This artifactual tail is present over the full interval and thus overlaps with the evoked EASSR in the time domain. Finally, the last subfigure shows the frequency domain representation of the EEG recording, which contains a distinct peak at the modulation frequency. Since the applied subthreshold stimulation level does not evoke an EASSR, this spectral peak is solely caused by the stimulation artifact. When comparing this subfigure with the frequency domain representation of the ASSR shown in [Figure 2.5](#), it becomes apparent why this artifact can result in a false positive detection and a distortion of the EASSR.

A discriminatory feature between the artifact and the (E)ASSR is their group delay or latency. Since the artifact is caused by the electrical stimulation of the CI, it propagates almost instantaneously from the stimulating device to the EEG-electrodes. In contrast, the generation of an EASSR exhibits a group delay or latency of about 40 *ms* for modulation frequencies in the 40 Hz range due to processing in the brain. This difference in latency will be used to evaluate the effectiveness of the artifact suppression methods in case EEG recordings in response to stimulation at different modulation frequencies are available. In that case, the group delay of the detected EASSRs can be evaluated and compared to the expected range of 40 *ms*. Note that the group delay is used instead of the phase, due to the ambiguous character of the latter.[\[38, 40\]](#)

The symmetrical stimulation signal does not contain a spectral component at the modulation frequency according to [\[14, 27, 40, 3\]](#). The stimulation artifact at this frequency is thus believed to originate from nonidealities and nonlinearities in the system. These statements are further analyzed in [Chapter 3](#).

The stimulation artifact at the modulation frequency displays a high intersubject variability and is present to some extent in all EEG channels. The morphology and the temporal extent of the artifact pulses mostly depend on the stimulation

parameters, although the impedance of the electrode-tissue interface, the body tissue, and the EEG recording electrode-gel-skin-interface also play an important role. Furthermore, the artifact is also affected by the EEG recording equipment and the preprocessing procedures. [14]

The remainder of this section will discuss the effect of four important factors which play a crucial role in the complexity of the EASSR detection problem.

A first factor is the **stimulation level**. An increased stimulation level results in larger stimulation artifacts. [16] For CIs of Cochlear Ltd., the stimulation amplitude is clinically expressed in current levels (CLs), which is a scale ranging from 0 up to and including 255. The relationship between CLs and amperes is logarithmic. The exact conversion depends on the device type, and is commonly given by [30]:

$$I_A = 17.5 \cdot 10^{-6} \cdot 100^{(I_{CL}/255)} \quad (2.2)$$

where I_A and I_{CL} represent the same electrical current expressed in amperes and current levels respectively. The dynamic range of the stimulation currents thus ranges from $17.5 \mu A$ to $1.75 mA$. The artifact suppression algorithms should be effective at every stimulation level.

A second important factor is the **stimulation mode**, as discussed in Section 2.2. MP mode stimulation results in a wider extent of the electromagnetic fields and thus larger electrical CI artifacts as compared to BP mode stimulation. [44, 32] Since MP mode stimulation is used in clinical practice, the EASSR detection methods must be effective for this stimulation mode.

A third factor is the **EEG recording electrode position**. The artifact is stronger in EEG channels located on the side of the head closest to the CI (ipsilateral side) than the opposite side (contralateral side). [14] Furthermore, despite the limited research about lateralization in unilateral CI subjects, [33] indicates responses may be lateralized to contralateral channels in unilateral CI subjects. This might ease the EASSR detection in contralateral channels in comparison to ipsilateral channels. [15] Moreover, in infants and children, which form an important target demographic for automated fitting procedures, the distinction between ipsi- and contralateral EEG-channels is less clear since all channels contain strong stimulation artifacts due to their smaller head size. [14] The EASSR detection methods should therefore be effective in all EEG channels.

A fourth and last factor is the **pulse rate** of the stimulation signal, which defines the number of pulses per second (pps). An artifact characterization study presented in [16] found that a pulse rate for 500 pps ($IPI = 2 ms$), the stimulation artifact duration varies from $0.7 ms$ to $1.7 ms$ in contralateral channels and from $0.7 ms$ to $2 ms$ in ipsilateral channels. This indicates that the end of the interpulse interval is not contaminated by the stimulation artifact. For a pulse rate of 900 pps ($IPI \approx 1.1 ms$), in contralateral channels, the median stimulation artifact duration equals $0.9 ms$, although in some subjects, it is close or equal to $1.1 ms$. In ipsilateral channels, the stimulation artifact duration equals $1.1 ms$ in most CI recipients in the study. [16]

Since a pulse rate of 900 pps is clinically used, and the determined T- and C-levels depend on the pulse rate, the EASSR detection should be effective for this pulse rate of 900 pps. [14, 35]

2.6 Artifact Suppression Algorithms

In order to reliably detect EASSR in EEG recordings of CI recipients, the stimulation artifact must be suppressed through signal processing algorithms. As motivated, the ideal artifact suppression method should be effective for stimulation at all stimulation levels, in MP mode stimulation, a pulse rate of 900 *pps*, in both ipsi- and contralateral EEG channels and preferably requiring only a single EEG channel to reliably detect the EASSR. Various algorithms have been developed and validated for different stimulation conditions. This section provides an overview of CI artifact suppression algorithms for EASSR detection and their performance. For each method, its working principle, crucial assumptions, performance, benefits and drawbacks are briefly considered. The performance is mentioned for EEG recordings acquired with a sample rate of 8192 Hz using the clinically relevant MP mode stimulation, unless stated otherwise. Table 2.1 provides an overview of the performance of these methods.

2.6.1 Linear Interpolation

The first artifact suppression method in this overview is referred to as linear interpolation (LI) and is widely used in literature. [25, 40, 16, 24] This method interpolates the EEG signal between a sample before and after the stimulation pulse. As the name suggests, often a linear interpolation is used; although cubic and spline interpolations have also been explored. [3] Variations on LI has also been studied, such as the Moving Strobe Averaging (MSA) algorithm which removes artifact-dominated samples prior to applying LI. [27]

This artifact suppression method assumes that samples before and after the stimulation pulse are not affected by the artifact, *i.e.* the stimulation artifact must have decayed before the next pulse occurs. [15] The results from the artifact characterization presented in [16] show that at a pulse rate of 500 pps, the stimulation artifact duration is lower than the interpulse interval; while at a pulse rate of 900 pps, the duration is only shorter in contralateral channels of some CI recipients.

These results are reflected in the performance: [14] found that LI is effective in both contra- and ipsilateral channels at a pulse rate of 500 pps; although the estimated latencies in the ipsilateral channels are centered around the lower bound of the expected range. Using a hyperrate EEG system, [40] showed that LI is effective in contralateral channels at 900 pps, but not in ipsilateral channels.

A main benefit of LI is that it only requires data originating from a single EEG channel. A drawback is that LI might result in interpolation artifacts in case the assumption is not satisfied, which might in turn amplify the stimulation artifact.

[27] Another disadvantage is its sensitivity to noise since only a limited number of samples are considered in the analysis.

2.6.2 Template Subtraction

A second method is referred to as template subtraction (TS) [15]. This artifact suppression method uses an EEG recording containing stimulation artifacts and no significant response to create a template of the stimulation artifact. In a subsequent step, this template is appropriately scaled and subtracted from another EEG recording to determine whether or not an EASSR is present. In [15], the artifact template is obtained at the correct stimulation level by modulating the stimulation pulse train at a modulation frequency which does not evoke an EASSR. However, the research paper mentions the use of subthreshold EEG recordings might be effective as well.

This method assumes the artifact is stationary over the course of the EEG recording, since only a single template is used. In case subthreshold EEG recordings are used for the template creation, assumptions about the scaling of the artifact must be made. [15]

In EEG recordings contaminated with artifacts due to stimulation at a pulse rate of 500 pps, [15] found that TS is effective in both contra- and ipsilateral channels.

The fact that TS only requires a single-channel EEG recording to determine whether an EASSR is present forms a large benefit. Additionally, the template construction is data-driven and does not require any prior knowledge about the stimulation artifact. This last argument is also a drawback, as no prior knowledge can be incorporated into the template construction. However, its largest disadvantage is the requirement of a stimulation artifact recording to construct the template, even though [15] mentions this recording can be reduced to 60 seconds without compromising on performance.

2.6.3 Independent Component Analysis

A third method applies Independent Component Analysis (ICA), a popular approach in the context of blind source separation. For the detection of transient auditory evoked potentials, ICA has been applied with success. [8, 20] For the detection of EASSRs, ICA is applied and evaluated in [17].

ICA assumes that stimulation artifact and EASSR are statistically independent. In practice, this assumption is most likely violated as the stimulation artifact and response both originate from the electrical stimulation and therefore show similar characteristics. [17]

ICA is able to detect EASSRs in both contra- and ipsilateral channels at a pulse rate of 500 pps. However, it must be noted that the EASSRs could be detected in contralateral channels without any form of artifact suppression. At a pulse rate of 900 pps, ICA failed to separate the EASSR from the stimulation artifact, except for two out of seven CI recipients. In general, [17] concluded that mixed results are obtained when using ICA for EASSR detection.

ICA does not require any prior knowledge, which is both a benefit and a drawback. Furthermore, ICA requires multi-channel EEG recordings, which are more expensive and increase the preparation time since more electrodes must be placed on the scalp. A last drawback is the identification of the artifact components. A manual selection of these components requires expertise, is subjective and time-consuming; an automatic selection on the other hand has to rely on assumptions that may not always hold in practice. [10, 17]

2.6.4 Kalman Filtering Approaches

A fourth approach is introduced in [34] and further extended in [14] and relies on a Kalman filter. The method uses an artifact model which consists of a number of artifact templates, which are constructed based on prior knowledge about the artifact. In the initial model, this artifact template was a triangular pulse [34]. In the extended model, an exponentially decaying tail, a stimulation pulse and a bias are included into the model. The decay rate of the exponentially decaying tail is estimated on the EEG recording. A Kalman filter is then used to determine the contribution of each artifact template and two additional response templates to the observed EEG recording at each time index.

This method assumes that the stimulation artifact can be accurately modeled as a combination of these artifact templates. Note the contrast with the template subtraction method, where the template is constructed in a more data-driven fashion.

In [34], the Kalman filter model is effective in contralateral channels in BP stimulation mode at a pulse rate of 900 pps. In [14], the extended Kalman filter model is effective in both contra- and ipsilateral channels at a pulse rate of 500 pps.

This method requires data from only a single EEG channel and does not assume stationarity of the EASSR or artifact. However, it has two disadvantages. First, the artifact model is not flexible, as it only includes a limited amount of artifact templates. Furthermore, the method is rather sensitive to the tuning of the noise covariance matrices. [14]

2.6.5 System Identification Approach

The last method in this overview is the system identification (SI) approach introduced in [40]. In this approach, the separation problem is presented as an SI problem. Both the stimulation artifact and the EASSR are modeled as the result of a filter operation of an input signal with an artifact and response FIR filter respectively. The FIR-coefficients are estimated through an ordinary least-squares (OLS) using three EEG recordings at distinct modulation frequencies. This method is detailed in [Subsection 5.7.1](#).

The assumptions of this method are rather limited. Prior knowledge about the stimulation artifact and the EASSR is incorporated in the input signal and the structure of their respective model.

The SI method has been shown to be effective in ipsi- and contralateral recordings at 900 pps. It is however important to note that a hyperrate EEG system with a sampling rate of 262144 Hz is used in the evaluation of this method.

The main benefits of this method are that it only requires single-channel EEG recordings and that it is also effective in ipsilateral EEG channels at a pulse rate of 900 pps, in contrast to all other methods mentioned. A drawback of the method is that three EEG recordings from a single channel at different modulation frequencies are required to disentangle the stimulation artifact from the EASSR. However, current research focuses on reducing the number of single-channel EEG recordings without compromising performance.

TABLE 2.1: Overview of the performance of existing artifact suppression methods. Results obtained using a hyperrate system are indicated with an asterisk.

Pulse Rate	Channel	Methods				
		LI	TS	ICA	Ex. KF	SI
500 pps MP	Contra.	Yes	Yes	Yes	Yes	-
	Ipsi.	Yes	Yes	Mixed	Yes	-
900 pps MP	Contra.	Yes*	-	Mixed	-	Yes*
	Ipsi.	No*	-	Mixed	-	Yes*

2.7 Conclusion

This chapter has provided a brief overview of the components and working principles of a cochlear implant. Subsequently, EEG is discussed and the details of its acquisition and preprocessing in the context of this thesis have been described.

This thesis aims to detect the electrically evoked auditory steady-state response (EASSR) in EEG recordings of CI recipients. However, its detection is hindered by the electrical artifact, which is caused by the stimulation of the CI and thus inevitable. [40] Both the RF communication and the stimulation itself contribute to this electrical artifact. In the context of EASSR detection, the artifact due to the stimulation is most relevant as it overlaps with the EASSR in both the time and frequency domain. [16] Furthermore, the effect of the stimulation parameters on the EASSR and stimulation artifact are considered. Artifact suppression methods should be effective at all stimulation levels, in monopolar (MP) mode stimulation, at a pulse rate of 900 pps, and in both contralateral and ipsilateral channels. [14, 16, 32] To evaluate the performance of these algorithms, the group delay or latency of the estimated EASSRs is determined. This latency is between 35 and 55 *ms* in case an EASSR has been detected, and close to zero in case an artifact is observed. [40, 38]

Lastly, an overview of existing artifact suppression methods is provided. The system identification method [40] is the only artifact suppression method which is effective under all stimulation conditions.

Chapter 3

Theoretical Artifact Analysis

3.1 Introduction

In normal hearing subjects, an ASSR can be objectively detected in the EEG at the modulation frequency in the frequency domain. However, in CI recipients, a spectral component at this frequency can also originate from the stimulation artifact. Therefore, observing a spectral peak at the modulation frequency in EEG recordings of CI recipients does not necessarily imply an EASSR is present, as illustrated in [Figure 2.6](#). This chapter analyzes under which conditions the stimulation signal used to evoke EASSRs contains such a spectral component at the modulation frequency.

The relevance of this analysis is twofold. First, in case the input signal does not contain a spectral component at the modulation frequency, the artifactual component at this frequency must be the result of nonlinearities in the system. Secondly, since the stimulation pulses are clearly visible in the EEG recording, its frequency spectrum is related to the spectrum of the observed stimulation artifact.

In literature, such a spectral analysis is typically conducted through simulations [[3](#), [16](#), [40](#)], or by loosely referring to theoretical results without presenting derivations [[27](#)]. In contrast, [Section 3.2](#) focuses on an analytical derivation of the temporal and spectral representation of the ideal stimulation signal, which is used in the simulations in literature. This approach allows to identify the factors which are able to exert an influence on the stimulation artifact at the frequency of interest. [Section 3.3](#) remarks that this ideal stimulation signal cannot be applied in practice due to the charge-balance constraint (see *infra*). Therefore, the representation of a practical stimulation signal is proposed and analyzed. Next, [Section 3.4](#) studies the potential effect of stimulus nonidealities and nonlinearities on the stimulation artifact at the modulation frequency. [Section 3.5](#) concludes the chapter by postulating three statements on the origin of the stimulation artifacts. All figures shown in this chapter result from analytical derivations and are validated through simulations in MATLAB.

3.2 Ideal Stimulation Signals

This section analyzes the ideal stimulation signals used in the CIs of Cochlear Ltd. Although the specifications of the stimulation signals may differ between different CI manufacturers, they do share common characteristics such as a pulsating nature and charge-balance for safety reasons. [51] Similar analyses can thus be conducted for those signals, but are outside the scope of this thesis.

Cochlear Ltd. uses a biphasic, cathodic-first pulse train to stimulate the auditory nerve. These pulses are presented at a stimulation, pulse, or carrier rate f_c . Through amplitude modulation (AM) of this pulse train with a sinusoidal signal oscillating at a modulation frequency f_m , an EASSR is elicited at this particular frequency. [14, 40] This section analyzes under which circumstances the ideal stimulation signal itself contains a spectral component at this modulation frequency f_m . All spectral representations shown in this section are verified using simulations in MATLAB.

3.2.1 Time-Domain Representation

First, a time-domain representation of the ideal stimulation signal is presented by subsequently considering an individual biphasic cathodic-first pulse, a pulse train, and a modulated pulse train.

A biphasic, cathodic-first pulse $p(t)$ can be represented in the time domain as:

$$p(t) = A_p \Pi\left(\frac{t - (\frac{T_p}{2} + \frac{T_i}{2})}{T_p}\right) + A_n \Pi\left(\frac{t + \frac{T_n}{2} + \frac{T_i}{2}}{T_n}\right) \quad (3.1)$$

in which A_p and T_p , and A_n and T_n represent the amplitude and duration of the positive and negative pulse respectively; T_i represents the interphase duration; $\Pi(\frac{t}{T})$ represents a rectangular box function of duration T , centered around the origin. In order to avoid tissue damage, DC-stimulation must be avoided. Therefore, both phases of the pulse have to be charge-balanced resulting in the charge-balance constraint [51]:

$$\int_{-\frac{T_n+T_i}{2}}^{\frac{T_p+T_i}{2}} p(t) dt = A_p T_p + A_n T_n = 0 \quad (3.2)$$

This biphasic, cathodic-first pulse $p(t)$ is repeated at the pulse f_c resulting in a stimulation pulse train $f(t)$:

$$f(t) = \sum_{k=-\infty}^{+\infty} p(t - kT_c) = p(t) * \sum_{k=-\infty}^{+\infty} \delta(t - kT_c) \quad (3.3)$$

in which T_c represents the carrier period, the reciprocal of the carrier frequency f_c .

This pulse train $f(t)$ is then modulated with a cosine oscillating at a modulation frequency f_m . The modulation amplitude, depth, and phase are represented by A_m , D , and ϕ_m respectively. This results in a final time domain representation of the ideal stimulation signal $g_{ideal}(t)$ applied to elicit an EASSR:

$$g_{ideal}(t) = f(t) \cdot m(t) = f(t) \cdot (A_m \cdot (1 + D \cdot \cos(2\pi f_m t + \phi_m))) \quad (3.4)$$

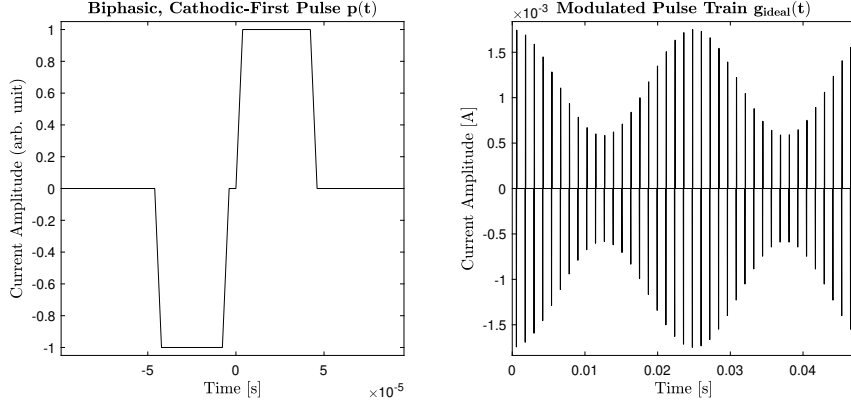


FIGURE 3.1: Time-domain representation of the ideal stimulation pulse (left) and ideal modulated signal (right)

Figure 3.1 shows the time-domain representation of a biphasic, cathodic-first, perfectly symmetrical pulse $p(t)$ and a modulated train $g_{ideal}(t)$ consisting of these pulses. Perfect symmetrical pulses imply that $T_p = T_n \triangleq T$ and $A_p = -A_n \triangleq A$. A pulse and interphase duration of $37 \mu s$ and $8 \mu s$ are used in both subfigures. The right subfigure has a maximal stimulation amplitude of 255 current levels, a modulation depth of 50%, a modulation frequency f_m of 40 Hz and a carrier frequency f_c of 900 Hz. All parameters are rounded to avoid spectral leakage.

In order to interpret the significance of all terms in the equations, typical values for CIs of manufacturer Cochlear Ltd are provided. Cochlear Ltd uses perfectly symmetrical pulses. [14] Typical values for the pulse duration T are $25 \mu s$ and $37 \mu s$. The interphase duration T_i is commonly $8 \mu s$. In this analysis, A is taken to be 1 such that all amplitude information is contained in the modulation amplitude A_m and depth D of the modulating signal $m(t)$. The pulse rate f_c is 900 Hz for clinically relevant stimulation strategies. Modulation frequencies f_m between 1 and 200 Hz can evoke ASSRs in normal-hearing individuals, but the response is most distinct in the 40 Hz range. [38]

3.2.2 Frequency-Domain Representation

Based on the time-domain representation presented in the previous subsection, a frequency-domain representation of the stimulation signal is derived by subsequently considering an individual biphasic cathodic-first pulse, a pulse train, and a modulated pulse train.

Since a rectangular box function corresponds to a sinc-function [13], the frequency spectrum $P(f)$ of a biphasic, cathodic-first pulse $p(t)$ corresponds to:

$$P(f) = A_p T_p \cdot \frac{\sin(\pi f T_p)}{\pi f T_p} \cdot e^{-j\pi f (T_p + T_i)} + A_n T_n \cdot \frac{\sin(\pi f T_n)}{\pi f T_n} \cdot e^{j\pi f (T_n + T_i)} \quad (3.5)$$

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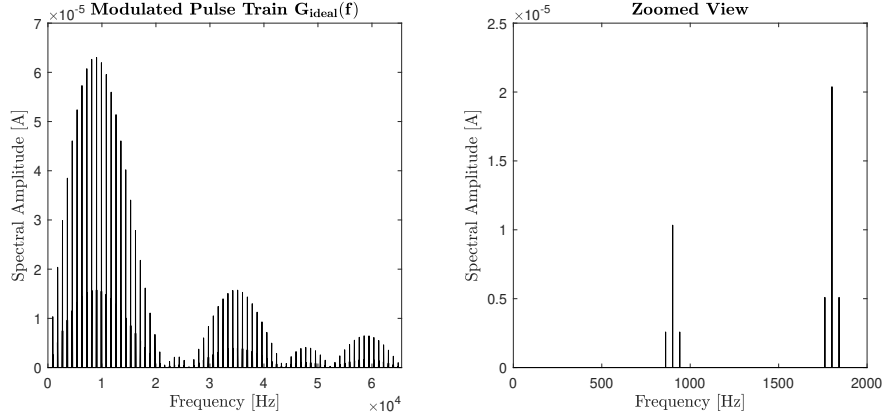


FIGURE 3.2: Frequency-domain representation of the ideal stimulation signal

Note that the pulse amplitudes and durations should satisfy the charge-balance constraint posed in [Equation 3.2](#). In case of a perfectly symmetric pulse, the spectral representation simplifies to:

$$P_{sym}(f) = -2AT \cdot \frac{\sin(\pi f T)}{\pi f T} \cdot (j \sin(\pi f (T + T_i))) \quad (3.6)$$

When a general biphasic, cathodic-first pulse $p(t)$ is repeated at a carrier frequency f_c , a periodic pulse train is obtained such that its frequency spectrum is discrete:

$$F(f) = P(f) \cdot f_c \sum_{k=-\infty}^{+\infty} \delta(f - k f_c) = f_c \sum_{k=-\infty}^{+\infty} P(f - k f_c) \quad (3.7)$$

This pulse train is then amplitude modulated with the sinusoidal modulating signal $m(t)$, of which the frequency spectrum corresponds to [\[13\]](#):

$$M(f) = A_m \cdot \delta(f) + \frac{A_m D}{2} \cdot (e^{j\phi_m} \delta(f - f_m) + e^{-j\phi_m} \delta(f + f_m)) \quad (3.8)$$

The amplitude modulation operation is modeled as a multiplication between $f(t)$ and $m(t)$ in the time domain. By the convolution theorem, the frequency representation of the ideal modulated pulse train $G_{ideal}(f)$ is given by convolving $F(f)$ with $M(f)$:

$$G_{ideal}(f) = F(f) * M(f) = A_m \cdot F(f) + \frac{A_m D}{2} (e^{j\phi_m} F(f - f_m) + e^{-j\phi_m} F(f + f_m)) \quad (3.9)$$

[Figure 3.2](#) shows the frequency-domain representation of the biphasic, cathodic-first, modulated pulse train $G_{ideal}(f)$ consisting of perfectly symmetrical pulses, and a zoom which focuses on the lower frequencies. The discrete nature of the latter originates from the repetition of pulses in the time domain, each main peak is accompanied by two peaks due to the amplitude modulation by the sinusoidal signal. The figure is created using the same parameters as in [Figure 3.1](#).

3.2.3 Spectral Components of Interest

It is especially relevant to analyze the spectral component of the ideal stimulation signal at the modulation frequency for the reasons mentioned in the introduction. The spectral component of the stimulation signal at the modulation frequency corresponds to:

$$G_{ideal}(f_m) = A_m \cdot F(f_m) + \frac{A_m D}{2} (e^{j\phi_m} F(0) + e^{-j\phi_m} F(2 \cdot f_m)) \quad (3.10)$$

Due to the discrete nature of the frequency spectrum of the pulse train $F(f)$, the first and last term are not able to contribute to the result as no Dirac pulse occurs at $f = f_m$ and $f = 2f_m$ since $f_m \neq kf_c$ and $2f_m \neq kf_c$ for integer k . A final expression for the frequency component at the modulation frequency is thus given by:

$$G_{ideal}(f_m) = \frac{A_m D}{2} e^{j\phi_m} F(0) = \frac{A_m D}{2} \cdot e^{j\phi_m} \cdot f_c \cdot (A_p T_p + A_n T_n) = 0 \quad (3.11)$$

where the last equality is due to the charge-balance constraint posed by [Equation 3.2](#).

Furthermore, it is relevant to determine whether the stimulation signal contains nonzero spectral components at the harmonics of the modulation frequency. Evaluating the obtained spectral representation $G(f)$ for positive integer multiples n strictly larger than one of the modulation frequency f_m results in:

$$G_{ideal}(nf_m) = A_m \cdot F(nf_m) + \frac{A_m \cdot D}{2} (e^{j\phi_m} F((n-1)f_m) + e^{-j\phi_m} F((n+1)f_m)) \quad (3.12)$$

As $F(nf_m)$ is zero for all nonzero integer n , [Equation 3.12](#) shows the stimulation signal does not contain any spectral energy at harmonics of the modulation frequency.

The fact that the ideal stimulation signal does not contain a spectral component at the modulation frequency or harmonics thereof is often mentioned in literature [\[3, 14, 27, 40\]](#), where the analysis is done through simulations. The absence of such spectral components in the input signal indicates that nonlinearities in the system are required to explain the stimulation artifact at the modulation frequency. [\[40\]](#)

3.3 Practical Stimulation Signals

The analysis of the ideal stimulation signal in [Section 3.2](#) assumes the pulses follow the sinusoidal profile of the modulating $m(t)$. This assumption is implicitly made when modeling the amplitude modulation of the pulse train as a multiplication. Although this assumption is omnipresent in literature [\[3, 40, 14, 27\]](#), it neglects that in practice each pulse will simply be scaled due to the limitations of the CI itself and the requirement to preserve charge-balance. The scaling operation means that each pulse preserves its rectangular shape. [Figure 3.3](#) shows an extract from the ideal and practical modulated pulse train. The ideal signal on the left follows the profile of the modulating signal, while the practical signal on the right is an appropriately scaled version of the generic pulse and is used in practice. Note that the ideal signal on the left violates the charge-balance constraint. A modulation frequency f_m of

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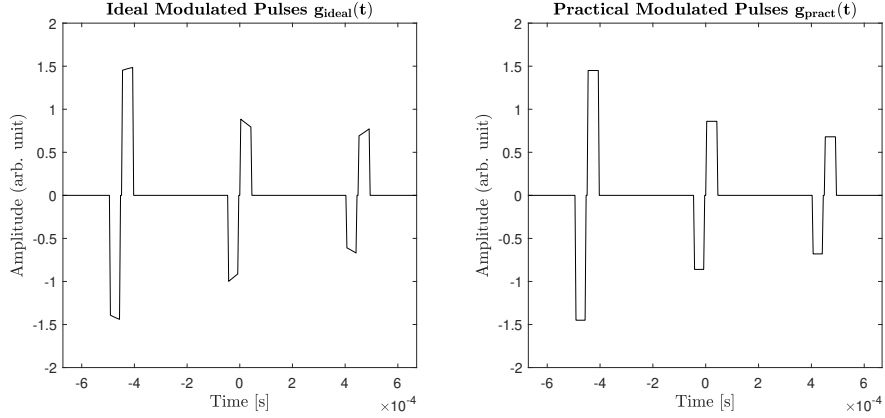


FIGURE 3.3: The different pulse profile between the ideal (left) and practical (right) stimulation signal

800 Hz is used to create this figure to exaggerate the differences, although similar differences occur for 40 Hz, albeit to a smaller extent due to the smaller steepness of the modulating signal $m(t)$. Again, all spectral representations shown in this section are verified using simulations in MATLAB.

3.3.1 Time-Domain Representation

The practical modulated pulse train $g_{pract}(t)$ can be described analytically in the time domain by adjusting the modeling of the amplitude modulation operation:

$$g_{pract}(t) = p(t) * (m(t) \cdot \sum_{k=-\infty}^{+\infty} \delta(t - kT_c)) \quad (3.13)$$

Note that instead of a multiplication, the modulation signal $m(t)$ now scales the Dirac pulses before the convolution with the pulse $p(t)$, such that a charge-balanced, practical modulated pulse train $g_{pract}(t)$ is obtained.

3.3.2 Frequency-Domain Representation

Based on the time-domain representation presented in the previous subsection, the frequency-domain representation can be derived. Using the convolution theorem, a general expression for the spectral representation of the practical modulated pulse train is obtained:

$$G_{pract}(f) = P(f) \cdot (M(f) * f_c \sum_{k=-\infty}^{+\infty} \delta(t - kT_c)) \quad (3.14)$$

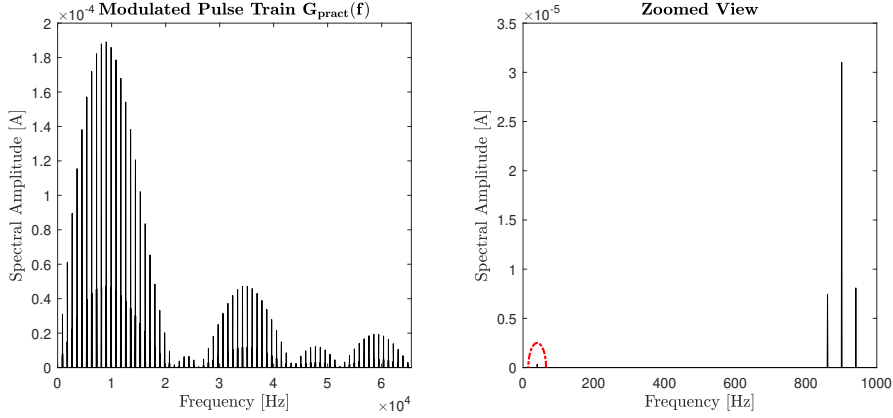


FIGURE 3.4: Frequency-domain representation of the practical stimulation signal. A circle has been drawn around the spectral component at the modulation frequency.

This expression can be expanded using the expression for $M(f)$ given by Equation 3.8:

$$G_{pract}(f) = P(f) \cdot A_m f_c \cdot \left(\sum_{k=-\infty}^{+\infty} \delta(f - k f_c) + \frac{D}{2} e^{j\phi_m} \sum_{k=-\infty}^{+\infty} \delta(f - f_m - k f_c) + \frac{D}{2} e^{-j\phi_m} \sum_{k=-\infty}^{+\infty} \delta(f + f_m - k f_c) \right) \quad (3.15)$$

Figure 3.4 shows the frequency representation of the practical stimulation signal, using the same parameters as Figure 3.1.

3.3.3 Spectral Components of Interest

The spectral component at the modulation frequency f_m in particular is of interest. Again, note that the first and last term of Equation 3.15 do not contribute to $G_{pract}(f_m)$ as the Dirac pulse trains do not contain a component at f_m or $2f_m$:

$$G_{pract}(f_m) = P(f_m) f_c \frac{A_m D}{2} e^{j\phi_m} \quad (3.16)$$

in which $P(f_m)$ is given by evaluating Equation 3.5:

$$P(f_m) = A_p T_p \cdot \frac{\sin(\pi f_m T_p)}{\pi f_m T_p} \cdot e^{-j\pi f_m (T_p + T_i)} + A_n T_n \cdot \frac{\sin(\pi f_m T_n)}{\pi f_m T_n} \cdot e^{j\pi f_m (T_n + T_i)} \quad (3.17)$$

Considering perfectly symmetrical pulses ($A_p = -A_n \triangleq A$, and $T_p = T_n \triangleq T$), and approximating $\sin(2\pi f_m (T + T_i)) \approx 2\pi f_m (T + T_i)$ and $\text{sinc}(\pi f_m T_p) \approx 1$ as $\pi f_m T$ is sufficiently small, Equation 3.6 can be simplified and evaluated for f_m :

$$P_{sym}(f_m) \approx -2ATj\pi f_m (T + T_i) \quad (3.18)$$

This results in an approximation for the expression of $G_{pract}(f_m)$:

$$G_{pract}(f_m) \approx AT\pi f_m(T + T_i)f_c A_m D e^{j\phi_m} e^{-j\frac{\pi}{2}} \quad (3.19)$$

This result shows that the practical stimulation signal does contain a spectral component at the modulation frequency when the practical constraints in the pulse generation are included in the analysis. It therefore shows that the presence of stimulation artifacts is inherent to the stimulation pulses themselves, and does not require nonidealities and nonlinearities in the stimulus generation process. The peak is visible in the theoretical spectrum shown in [Figure 3.4](#). Its amplitude is expressed in amperes. Since the electrode impedance is in the order of kOhm, [\[49\]](#) the resulting voltage is in the order of mV when no attenuation is taken into account.

Through a similar analysis as in the previous section, it can be shown that this practical stimulation signal does not contain spectral components at harmonics of the modulation frequency, as expected.

3.4 Effect of Nonidealities and Nonlinearities

Although [Section 3.3](#) has shown that system nonidealities and nonlinearities are theoretically not required for stimulation artifacts to be present, they are thought to amplify the inherent stimulation artifact. [\[16, 40\]](#) Therefore, this section considers whether nonidealities and nonlinearities contribute to the spectral component at the modulation frequency. The results from this theoretical analysis can provide guidance for the design of experiments used in the characterization of the stimulation artifact, and for the development of artifact models in EASSR detection algorithms.

3.4.1 Charge-Imbalance

The first analysis is concerned with the effect of pulse charge-imbalance. [\[16\]](#) has observed that the artifactual stimulation pulses in the EEG recordings can be asymmetrical. Causes which contribute to this asymmetry are assumed to lie in the limitations of the electronics generating the pulses [\[28\]](#), system nonlinearities [\[40\]](#), or a difference between the impedance of the active and reference electrode [\[14\]](#).

For the ideal modulated pulse train $g_{ideal}(t)$, the effect of an asymmetry in the pulses $p(t)$ on the stimulation artifact at the modulation frequency can directly be evaluated by considering $G_{ideal}(f_m)$:

$$G_{ideal}(f_m) = \frac{A_m D}{2} e^{j\phi_m} F(0) = \frac{A_m D}{2} e^{j\phi_m} f_c (A_p T_p + A_n T_n) \quad (3.20)$$

This result shows that the stimulation artifact at the modulation frequency is proportional to the charge-imbalance $A_p T_p + A_n T_n$, or in more general terms, to any DC-component $F(0)$ of the pulse train $f(t)$. In the frequency domain, this can be understood as the amplitude modulation with a sinusoidal signal shifts the DC-component to the modulation frequency. In this manner, a charge-imbalance

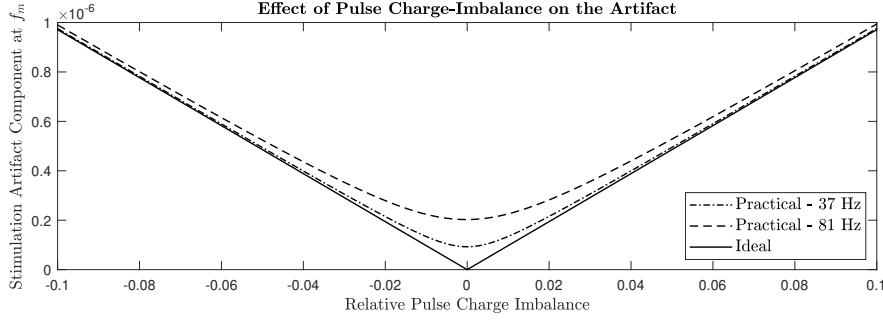


FIGURE 3.5: Effect of charge-imbalance on the stimulation artifact at the modulation frequency

results in an artifact contribution at this particular frequency. Note that this artifact contribution is independent of the modulation frequency f_m .

For the practical modulated pulse train $g_{pract}(t)$, the effect of a charge-imbalance can be analyzed by inspecting Equation 3.19. As this equation is rather involved, the effect of the charge-imbalance on the stimulation artifact at the modulation frequency has been visualized in Figure 3.5. This figure displays the absolute value of the spectral component at f_m of the ideal and practical modulated pulse train as a function of the relative pulse charge imbalance, defined as:

$$\text{Relative Pulse Charge Imbalance} = \frac{A_p T_p + A_n T_n}{AT} \quad (3.21)$$

The figure is created for a modulation frequency f_m of 37 Hz and 81 Hz, a carrier frequency of 900 Hz, a stimulation amplitude of 255 CLs, a modulation depth of 50%, a pulse width of 37 μs and by varying A_p from 0.9 to 1.1. A similar figure is obtained by varying the pulse duration T_p , but is not shown to avoid redundancy.

Note that whereas $G_{ideal}(f_m)$ is independent of the modulation frequency f_m , $G_{pract}(f_m)$ scales approximately linear with f_m , as long as $\pi f_m T$ is sufficiently small such that $\sin(\pi f_m T) \approx \pi f_m T$ holds approximately. The scaling of the artifact with the modulation frequency can also be observed in Figure 3.5. For modulation frequencies in the range of interest, around 40 Hz, the difference between the ideal and practical pulses becomes negligible when a relative pulse charge-imbalance of two percent is present. For small charge-imbalances or relatively high modulation frequencies, the difference between the ideal and practical stimulation signal can no longer be neglected.

In [22], a modulating signal containing multiple distinct modulation frequencies is used in the stimulation (albeit in an interleaved fashion). The stimulation artifact indeed seems to increase with the modulation frequency, as expected based on the practical stimulation signal analysis.

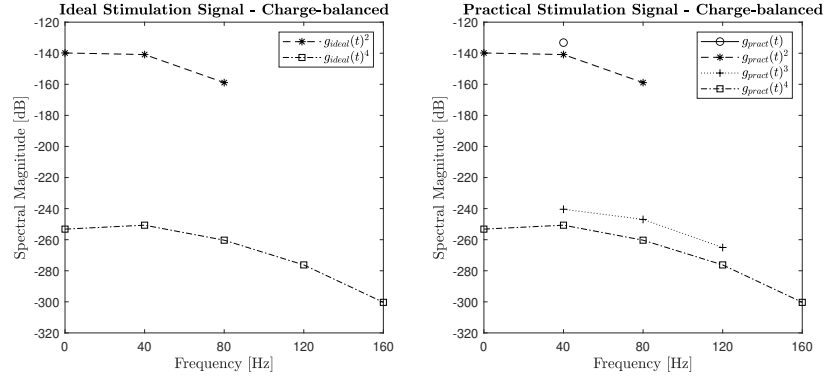


FIGURE 3.6: Effect of static polynomial non-linearities on the relevant spectral components, expressed in dB normalized to 1 A

3.4.2 Polynomial Non-Linearities

In literature, another imperfection considered as an important source for the stimulation artifact is the presence of nonlinearities. [40] The previous sections have shown that neither the ideal nor the practical stimulation signal inherently contains spectral components at harmonics of the modulation frequency. This section analyzes the effect of static polynomial nonlinearities on the stimulation signals. In contrast to the preceding sections, the mathematical derivations are rather cumbersome and do not increase insight into the results. The derivations behind all figures shown in this subsection are therefore included in [Appendix A](#).

The conclusion from the mathematical derivations is displayed in [Figure 3.6](#), which shows the spectral magnitudes at DC, the modulation frequency, and harmonics thereof up to and including the fourth order. The left subfigure shows the results for the ideal modulated pulse train, whereas the right subfigure displays the results for the practical modulated pulse train. Note that these figures are the result of an analytical spectral analysis, rather than simulations. As discussed in [Subsection 3.4.1](#), the ideal charge-balanced modulated pulse train does not contain any spectral component at the modulation frequency. Only when the stimulation signal is raised to an even order, a component at the modulation frequency appears. In contrast, when the practical modulated pulse train is observed, both odd and even powers contribute to the spectral component at the modulation frequencies. Based on these results, it can be concluded that only first and second order polynomial nonlinearities are able to significantly contribute to the stimulation artifact at the modulation frequency.

3.4.3 Combined Effect

In practice, the charge-imbalance and static polynomial nonlinearity might occur simultaneously. [Figure 3.7](#) shows the stimulation artifact at the modulation frequency for $g_{pract}(t)$ and $g_{pract}(t)^2$ in the left and middle subfigure respectively as a function

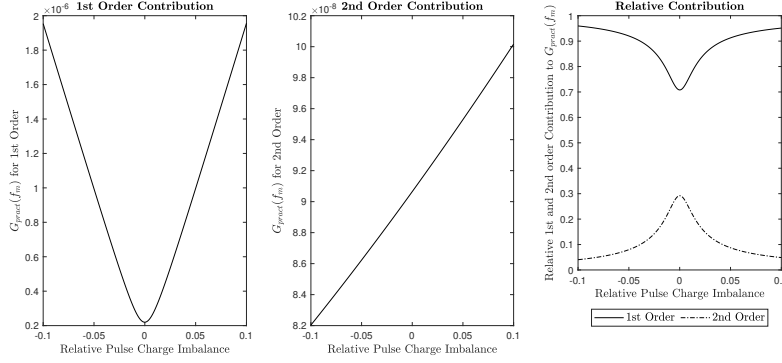


FIGURE 3.7: Combined effect of charge-imbalance followed by a static second order nonlinearity for the practical stimulation signal

of relative pulse charge imbalance. Note the difference scales on the y-axis. The right subfigure shows the relative contribution of the first and second order to this stimulation artifact, again as a function of the relative pulse charge imbalance. It reveals that the effect of second order nonlinearities becomes negligible when a sufficiently large charge imbalance is observed.

3.5 Conclusion

This chapter has studied the stimulation artifact from a theoretical point of view, with a strong emphasis on its spectral component at the modulation frequency. Section 3.2 has shown that the ideal stimulation signal does not contain an artifactual component at the modulation frequency; a result which is often presented in literature [16, 40], and implies the artifact must therefore originate from nonidealities and nonlinearities. Section 3.3 has refined this analysis by including the practical constraints into the analysis. These practical stimulation signals do show an inherent artifact component. This indicates that although nonidealities and nonlinearities might amplify the stimulation artifact, they are theoretically not required. Section 3.4 has studied the effect of nonidealities and nonlinearities on the stimulation artifact at the modulation frequency. These effects are capable of magnifying the observed stimulation artifact.

In summary, the analyses result in three statements about the stimulation artifact:

1. The stimulation artifact at the modulation frequency f_m is inherent to the practical stimulation signal, which is a more accurate description of the stimulation signal as it includes the practical constraints.
2. Any form of charge-imbalance results in a magnification of the stimulation artifact, and decreases the difference between stimulation artifact amplitudes at different modulation frequencies.
3. In the class of static polynomial nonlinearities, only the second order nonlinearities are able to contribute significantly to the stimulation artifact at the modulation frequency in case a limited amount of charge-imbalance is observed.

Chapter 4

Experimental Artifact Analysis

4.1 Introduction

Chapter 3 has analyzed the artifact from a theoretical point of view, upon which it has formulated three statements about the nature of the stimulation artifact:

1. The stimulation artifact at the modulation frequency f_m is inherent to the practical stimulation signal, which is a more accurate description of the stimulation signal as it includes the practical constraints.
2. Any form of charge-imbalance results in a magnification of the stimulation artifact, and decreases the difference between stimulation artifact amplitudes at different modulation frequencies.
3. In the class of static polynomial nonlinearities, only the second order nonlinearities are able to contribute significantly to the stimulation artifact at the modulation frequency in case a limited amount of charge-imbalance is observed.

This chapter aims to experimentally analyze the artifact in order to verify whether the practical stimulation signal is a more accurate model for the observed artifact, and to quantify to which degree the described nonidealities and nonlinearities actually occur in practice. **Section 4.2** discusses the materials and methods. **Section 4.3** displays the experimental results, which are further discussed in **Section 4.4**. Finally, **Section 4.5** concludes this chapter by reflecting upon the theoretical statements.

4.2 Materials and Methods

This section starts by considering the experimental set-up and the validity thereof, after which it discusses three methods to analyze and interpret the measured signals.

The necessity for an experimental set-up arises from the inability to acquire EEG recordings of CI recipients at high stimulation levels which solely contain stimulation artifacts, since the strong stimulation evokes an EASSR in the subject. Furthermore, applying stimulation levels which exceed the comfortable level is unethical. For these reasons, EEG recordings obtained by stimulating below the hearing threshold

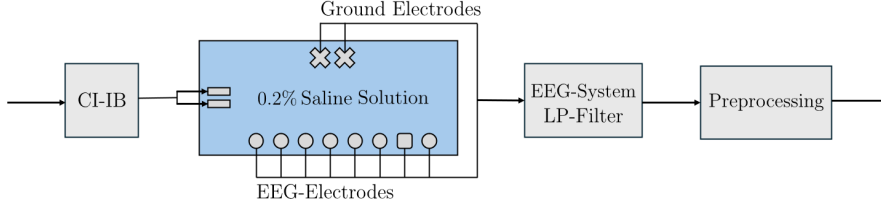


FIGURE 4.1: Overview of the Experimental Set-up

can be considered for artifact characterization purposes, as they do contain the stimulation artifact without any EASSR. However, nonlinearities are expected to be most pronounced at higher stimulation levels, far above the threshold level. An experimental set-up which uses a head phantom allows to use high stimulating levels for artifact characterization without eliciting EASSRs.

4.2.1 Experimental Set-up

A diagram of the experimental set-up is displayed in [Figure 4.1](#). The head phantom consists of a container of dimensions approximately 28 cm by 24 cm, filled with four liters of a 0.2% saline solution. A CI-in-a-box (CI-IB), containing a CIC4 implant of manufacturer Cochlear Ltd., is used to evoke the stimulation signals. The stimulation signals are applied to electrode 15, which is located towards the center of the electrode array, using MP mode stimulation. The stimulation and ground return from the CI-IB are attached via cables to the short side of the container. Along the long side of the container, eight EEG recording electrodes are attached facing away from the container side. The first electrode is positioned at a distance of four centimeters from the stimulation electrodes, as measured along the long side of the container. The subsequent electrodes are placed with an interelectrode distance of two centimeters. The distance between the stimulation and the last EEG recording electrode is 18 centimeters, corresponding to the average diameter of the human head [7]. All electrodes are regular EEG electrodes, except for the seventh which is a mastoid EEG electrode as indicated by the rounded square in [Figure 4.1](#). Two ground electrodes of the EEG recording system are located along the long container side opposite to the EEG recording electrodes. The acquisition and preprocessing of the EEG signals is performed according to the methodology mentioned in [Subsection 2.3.2](#).

In order to obtain measurements which are representative for artifact propagation throughout the human head, all system components must be approximated in the phantom. The CI-IB is identical to the clinically used CIs. The EEG electrode-tissue and -scalp interfaces are approximated and replaced by EEG electrode-saline-solution interfaces. The effects of artifact propagation throughout the human head are modeled by the 0.2% saline solution. Although other head phantoms for CI artifact characterization purposes have been proposed and utilized in literature, ranging from watermelons [2] to turkeys [32], the saline solution is selected for two reasons. First and most importantly, [29] found that a 0.2% saline solution is a stable representation for the intracranial volume in head phantoms for bio-electromagnetic

applications. Secondly, recordings in this medium have shown success in terms of artifact characterization of CI, albeit for devices of manufacturer Med-El in [27]. Further note that the same EEG and electrical equipment is used as in the acquisition of EEG recordings of CI recipients.

4.2.2 Stimulation Signals and Preprocessing

The experimental characterization of the stimulation artifact of the CI device is severely complicated as only cathodic- or anodic-first, biphasic, charge-balanced pulses can be applied as an input signal to the device. This renders more advanced system identification methods inapplicable as they often rely on specific input signal such as pure sinusoidal signals. [41]

In order to obtain measurements representative for stimulation artifacts evoked for clinically relevant stimulation parameters, a cathodic-first, biphasic, charge-balanced pulse train of 900 pulses per second (pps) is applied to the CI-IB. This pulse train is amplitude modulated with a sum of two cosines each oscillating at distinct frequencies, with a total modulation depth of 50 current levels. These frequencies are selected to be 37 Hz and 81 Hz. The former frequency falls inside the frequency range of interest, the latter is selected such that the potential second order nonlinear difference frequency at $81 - 37 = 44$ Hz is located in the frequency range of interest. Note that the selection of relatively prime integers for the frequencies is beneficial in the estimation of nonlinear components, since no higher order components can be present at frequencies where a first order components are dominant. A formal proof for this statement is provided in [6].

Ten measurements are carried out. In each measurement, the input signal is linearly scaled such that it covers a different amplitude range. The maximal stimulation levels of these input signals range between 167 and 255 current levels, which is the maximal stimulation level.¹ Figure 4.2 shows the modulating signal with a maximum of 255 CLs which will amplitude modulate the practical stimulation pulse train in microamperes, both in the time (left) and frequency (right) domain. Note that the spectral magnitude at both modulation frequencies is equal. Ten measurements were carried out for modulating signals oscillating at a single frequency, both for 37 Hz and 81 Hz. These measurements are not used for further analysis.

The preprocessing procedures are identical to those mentioned in Subsection 2.3.2. Since an EEG electrode measures a biopotential signal, the signal must be referenced to another electrode. In EEG recordings of CI recipients, central electrodes are typically selected as reference electrodes to avoid the introduction of a lateralization bias [31]. In this experimental set-up, the reference electrode is selected such that it contains as little artifact as possible. Consequently, any observed artifact at an analysis electrode indicates the presence of an artifact at that electrode position.

¹The applied maximal stimulation levels, expressed in current levels, are 167, 177, 187, 197, 206, 216, 226, 236, 245 and 255. Originally, 20 current levels were uniformly spaced between 70 and 255 current levels using MATLAB's `linspace`-command. The lowest ten were not applied as subthreshold EEG recordings of CI recipients are available for artifact characterization in this stimulation range.

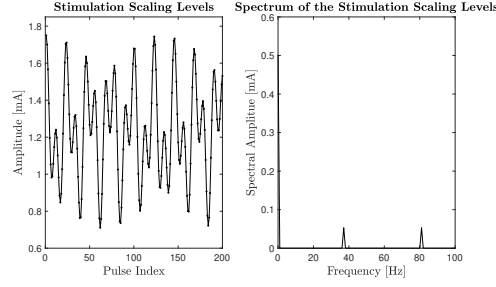


FIGURE 4.2: Applied stimulus, expressed in microamperes and current levels

Hence, the electrode positioned furthest from the stimulation electrodes is selected as the reference electrode.

Due to the design of the experimental set-up, the measured signals are intrinsically multidimensional such that they can be analyzed across time, frequency, spatial location, epochs, and stimulation levels. The analyses discussed in the following three subsections aim to exploit this multidimensional nature to characterize the artifact and study the hypotheses.

4.2.3 Analysis 1: Spectral and Temporal Characteristics

A first analysis focuses on the spectral and temporal characteristics of the measured stimulation artifact. First, it evaluates the spectrum of the mean epoch of the measured signal at each recording electrode, referenced to the last electrode as motivated earlier. This analysis considers the signals measured in response to the stimulation at the maximal stimulation level of 255 CLs, as nonlinearities are typically more pronounced at these higher stimulation levels.

The presence or absence of spectral peaks is evaluated at frequencies of interest, that is, those associated with linear characteristics (f_{m1}, f_{m2}), and second order ($2f_{m1}, 2f_{m2}, f_{m1} + f_{m2}, f_{m1} - f_{m2}$) and third order nonlinearities ($3f_{m1}, 3f_{m2}, f_{m2} - 2f_{m1}, f_{m2} + 2f_{m1}, 2f_{m2} + f_{m1}, 2f_{m2} - f_{m1}$). The statistical significance of the spectral component at each mentioned frequency will be determined using a one sample Hotelling's T^2 Test. Such an analysis compares the amplitude and phase at the frequency of interest in the mean epoch to the variance across all epochs. [40, 38] A significance level of five percent is used. In case the determined p -value for a specific frequency component exceeds this significance level, it does not differ from the noise and is therefore not identified as a peak in the spectrum.

In the time domain, the profile of the artifact pulses is evaluated by inspecting them before and after normalization to the maximal positive amplitude of each pulse.

In the context of the first theoretical statement about the artifact, this analysis is able to indicate the presence of the stimulation artifacts at the modulation frequencies. Furthermore, the profile of the artifact pulses indicates whether the profile of ideal or practical representation is a more accurate description. In the context of the third statement, this analysis is able to detect the presence of nonlinearities in the system.

4.2.4 Analysis 2: Presence and Nature of Pulse Asymmetry

A second analysis studies the potential asymmetry of the pulses. The theoretical analysis in [Chapter 3](#) shows that any charge-imbalance magnifies the stimulation artifact at the modulation frequency, regardless of whether ideal or practical stimulation signals are considered. The second analysis therefore evaluates whether a charge-imbalance is present, and what its nature is. In order to quantify this charge-imbalance, a pulse asymmetry measure is defined as:

$$PA(p) = \max_t x(t, p) + \min_t x(t, p) \quad (4.1)$$

where $x(t, p)$ represents the p -th pulse of the measured signal. This measure is similar to the "CI artifact amplitude"-measure as defined in [\[16\]](#), where the absolute value of $PA(p)$ is taken, after which it is averaged over all stimulation pulses of the recording to obtain a single measure per recording. [\[16\]](#) In the context of this analysis, it is assumed that the pulse widths, T_p and T_n in the terminology of [Chapter 3](#), are equal such that this measure is indeed indicative for the charge-imbalance.

Instead of averaging, this analysis studies the variation of the pulse asymmetry measure over the pulses. In the ideal case of perfect symmetry, $PA(p)$ is a zero signal. Any deviation from a zero signal can be used to characterize the nature of the asymmetry and is further studied in the frequency domain. A DC-component of this signal indicates that there is a constant pulse asymmetry in the measured signal. Spectral peaks at the modulation frequencies f_{m1} and f_{m2} indicate an asymmetry in the pulse form itself, *i.e.* $A_p \neq -A_n$ in the terminology of [Chapter 3](#). Spectral peaks at frequencies associated with nonlinearities indicate nonlinear scaling is involved.

The computation of the pulse asymmetry measure $PA(p)$ essentially downsamples the signal to the carrier frequency or pulse rate f_c . To avoid aliasing, the measured EEG signal is low-pass filtered before analysis using MATLAB's `lowpass` with a corner frequency of half the carrier frequency. Similar to the first analysis, the statistical significance of the spectral peaks at the frequencies of interest is evaluated using a Hotelling T^2 test with a significance level of five percent.

In the context of the second statement, this analysis is indicative of the presence of a charge-imbalance, and its nature. With respect to the third statement, a potential nonlinear scaling indicates their involvement in the system.

4.2.5 Analysis 3: Stimulation Artifact Scaling Analysis

The data acquired in this experimental set-up is multidimensional which enables to analyze how the magnitude of the stimulation artifact at the modulation frequencies varies over distance and stimulation level. Therefore, the third analysis will fit an appropriate surface through observed artifact magnitude at the modulation frequencies as a function of distance and stimulation level.

The scaling of these spectral components over distance and stimulation levels can be related to the variation of the root mean square (RMS) value of the measured EEG

signals and the mean normalized pulse asymmetry. The RMS-value is a measure of the power of the signal. The mean normalized pulse asymmetry is a relative measure to indicate the degree of asymmetry in the pulses of each EEG signal. It is computed by normalizing the pulse asymmetry measure $PA(p)$ of each pulse to the absolute value of the minimum of that pulse, after which it is averaged to obtain a single measure for each EEG signal. Therefore, it represents the mean asymmetry in the signal, *i.e.* $A_p + A_n$ in the terminology of [Chapter 3](#).

In the context of the first statement, the amplitude difference between the artifact components at the f_{m2} - and f_{m1} -component allows to evaluate whether the practical stimulation signal is a more accurate description. The presence of these components in the absence of an asymmetry indicates the artifact is inherent to the input signal. In the context of the second statement, the analysis shows how the relative pulse asymmetry varies with stimulation level and distance. The variation of these measures can be compared to the overall variation of the RMS-value of the signal.

4.3 Results

This section displays the results of the described analyses. The recorded EEG signals from the mastoid electrode (the seventh electrode from the stimulation electrodes) are excluded from the analysis as they exhibit severe distortion. This behaviour is most likely caused by an electrode defect.

4.3.1 Analysis 1: Spectral Analysis

[Figure 4.3](#) displays an overview of the statistically significant linear (1^{st} order components) and nonlinear (2^{nd} and 3^{rd} order) components in the frequency spectrum of the mean epoch of each electrode at the maximal stimulation level of 255 CLs. Fourth and higher orders are not analyzed, as no distinct peaks were observed in the spectrum. The first order components are present at each recording electrode. The spectral amplitude of the peak at f_{m2} is larger than f_{m1} , both of which decay exponentially over distance. The second order intermodulation components are present over all recording electrodes, while the second order harmonics are absent. Among the third order components, the peak associated with $2f_{m2} + f_{m1}$ is the only component which displays a consistent presence over the first five electrodes. The EEG signal measured at the third electrode, located at eight centimeters from the stimulation electrode, is further analyzed due to its pronounced linear and nonlinear contributions.

[Figure 4.4](#) shows the spectrum of the mean epoch at the third electrode. The statistically significant spectral peaks are indicated. The left subfigure of [Figure 4.5](#) shows a single biphasic, cathodic-first pulse of the mean epoch at the third recording electrode. The right subfigure shows an overlay of all measured pulses in this signal, each normalized to its maximum pulse amplitude such that the normalized positive pulse amplitude equals one. A flat profile is observed, as well as an asymmetry.

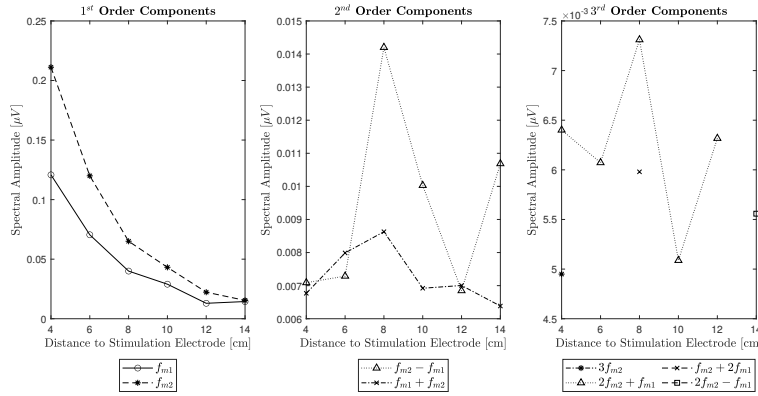


FIGURE 4.3: Statistically significant linear (1st order) and nonlinear (2nd and 3rd order) spectral components of the mean epochs in function of distance to the stimulation electrode at maximal stimulation level

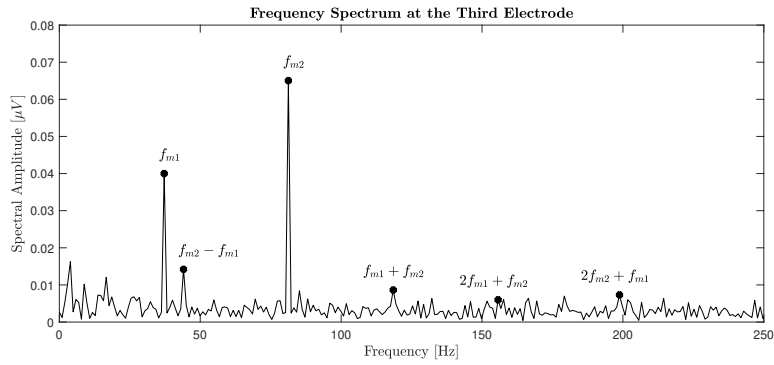


FIGURE 4.4: Frequency spectrum of the mean epoch at the third recording electrode; statistically significant components are indicated

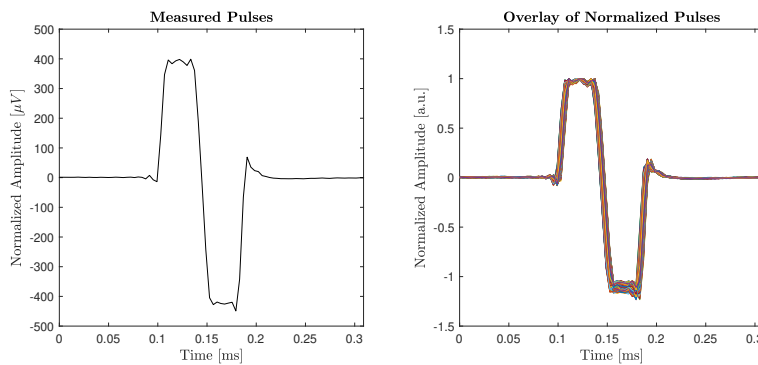


FIGURE 4.5: A single pulse of the mean epoch at the third recording electrode (left), and an overlay of all normalized pulses in this signal (right)

4.3.2 Analysis 2: Pulse Asymmetry Measure

Figure 4.6 shows the DC-component (0^{th} order component), linear (1^{st} order components) and nonlinear (2^{nd} and 3^{rd} order) components of the frequency spectrum of the pulse asymmetry signal $PA(p)$ at each electrode at maximal stimulation level, referenced to the last electrode. The first order components are approximately equal in magnitude present at all recording electrodes, and displays an exponentially decaying behavior over distance. The second order intermodulation components are present. An increased number of third order components is observed compared to the previous analysis, although the peak associated with $2f_{m2} + f_{m1}$ is the only component which displays a consistent presence over all electrodes. Again, the pulse asymmetry signal measured at the third electrode, located at eight centimeters from the stimulation electrode, is further analyzed due to its pronounced linear and nonlinear contributions.

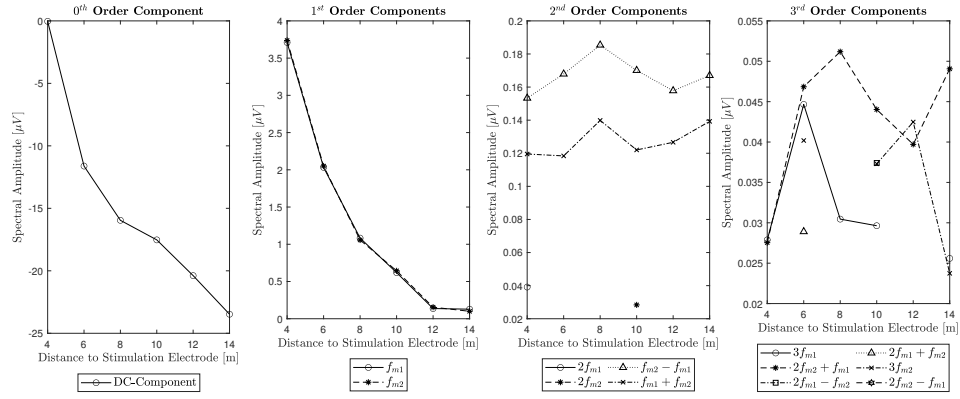


FIGURE 4.6: Statistically significant linear (1^{st} order) and nonlinear (2^{nd} and 3^{rd} order) of the pulse asymmetry signals in function of distance to the stimulation electrode at maximal stimulation level

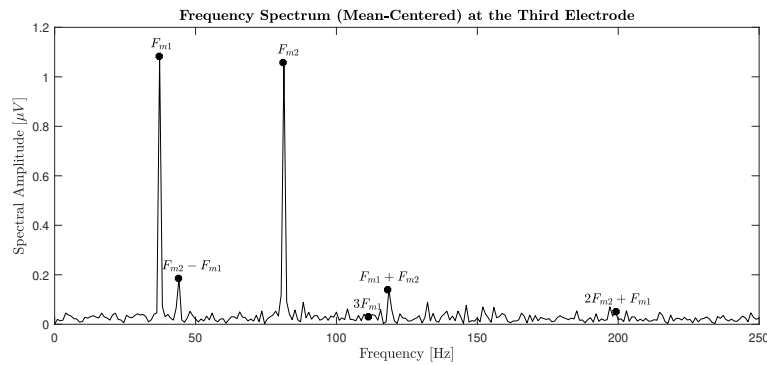


FIGURE 4.7: The pulse asymmetry signal (left) and its frequency spectrum after mean centering (right); statistically significant components are indicated

Figure 4.7 shows the frequency spectrum of the pulse asymmetry signal measured at the third recording electrode. The mean of this signal, which equals $-15.96 \mu V$, is subtracted the signal for presentation purposes. The first and second order components are clearly present, the third order components are less pronounced despite their statistical significance.

4.3.3 Analysis 3: Multivariate Fit

Figure 4.8 shows the fitted surface through the stimulation artifact amplitude at the modulation frequencies f_{m1} and f_{m2} as a function of the stimulation level and distance to the stimulation electrodes. At low stimulation levels, the artifact amplitude at these frequencies is non-significant for the last two electrodes. The spectral component at f_{m1} and f_{m2} are statistically significant in 54 and 55 out of 60 EEG recordings respectively. Non-significant values are not included in this analysis.

Figure 4.9 shows the fitted surface through the RMS-values and the mean normalized pulse asymmetry.

The stimulation artifact amplitudes at the modulation frequencies, the RMS-values, and the mean normalized pulse asymmetry show an exponential relationship with increasing distance to the stimulation electrode, and a predominantly linear relationship with the stimulation level. The fitted surface is therefore modeled as:

$$h(x, y; A, B, C, D) = (A \cdot \exp(Bx)) \cdot (Cy + D) \quad (4.2)$$

in which x represents the distance to the stimulation electrode in centimeters, and y the stimulation level in mA . The coefficients A , B , C and D are fit through MATLAB's `lsqcurvefit`. The resulting parameters, the R^2 -value, and the RMS error of the fit are shown in Table 4.1.

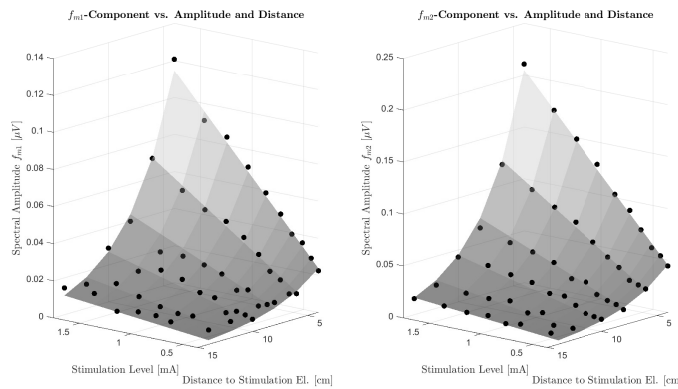


FIGURE 4.8: The magnitude stimulation artifact at f_{m1} (left) and f_{m2} (right) as a function of stimulation level and distance to the stimulation electrodes.

4. EXPERIMENTAL ARTIFACT ANALYSIS

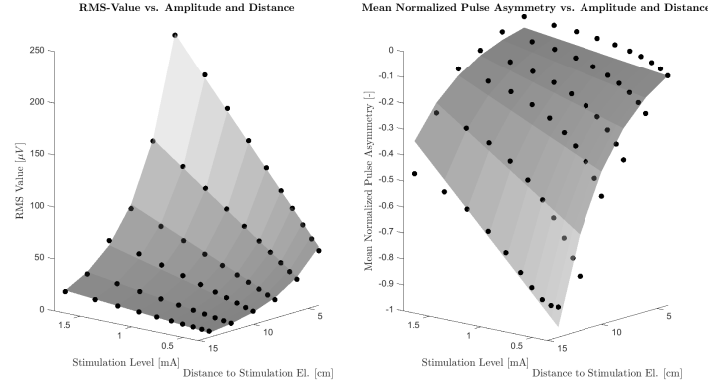


FIGURE 4.9: The RMS-value (left) and mean normalized pulse asymmetry (right) as a function of stimulation level and distance to the stimulation electrodes.

TABLE 4.1: Parameters, R^2 -values and RMS error of the fitted surfaces

Parameters	A	B	C	D	R^2 -value	RMS Error
Value f_{m1} -fit	0.599	-0.241	285.965	0.0010	0.98187	0.00323
Value f_{m2} -fit	1.093	-0.253	289.217	0.111	0.99378	0.00342
RMS-value	8.774	-0.2641	41417	3.5276	0.99833	2.01580
Normalized PA	0.064	0.2124	364.085	-0.912	0.95724	0.05355

4.4 Discussion

This section discusses and interprets the results as presented in the previous section. This discussion reflects upon the three statements about the stimulation artifact, as mentioned in [Section 3.5](#) and the introduction of this chapter.

4.4.1 Analysis 1: Spectral Analysis

With respect to the first statement about the artifact, this analysis shows clear artifact components at the modulation frequencies. This clearly indicates the problem of CI artifact contamination in the context of EASSR detection. At all recording electrodes except for the last one, the artifact amplitude is larger at f_{m2} than at f_{m1} . These amplitude differences are an indication that the practical stimulation signal shown in [Equation 3.13](#) is a more accurate model. Its spectral component shown in [Equation 3.19](#) predicts a stimulation artifact which scales with the modulation frequency. The component of the ideal stimulation signal shown in [Equation 3.11](#) does not predict any amplitude difference. Strictly speaking, this amplitude difference can also be explained due to a difference in signal attenuation at both frequencies. The flat profile of the pulses validates the assumption made in the practical stimulation signal analysis.

In the context of the third statement about the artifact, the second order nonlinearities are clearly present. This indicates second order nonlinearities are involved in the system. The sparse presence of the third order components indicates these components are absent or fall below the noise floor.

4.4.2 Analysis 2: Pulse Asymmetry Measure

With respect to the second statement, the DC-component of the pulse asymmetry signal shows there is a constant asymmetry in the pulses. The first order components are present as well, indicating that this asymmetry scales linearly with the stimulation amplitude of the pulse. Note that the amplitudes of these first order components are very similar, reflecting their equal spectral amplitude in the modulating signal shown in [Figure 4.2](#) of the input signal. These similar amplitudes imply both frequency components experience a similar attenuation. Therefore, the amplitude difference of the spectral components as observed in the first analysis is not caused by attenuation, but due to the nature of the spectrum as predicted by the practical stimulation signal representation.

In the context of the third statement, the second and third order components indicate that the artifactual stimulation pulses in the EEG recording display nonlinear scaling behavior.

4.4.3 Analysis 3: Multivariate Fit

With respect to the first statement, the stimulation artifacts at the modulation frequencies are statistically significant in almost all EEG recordings. This is indicative that the stimulation artifact is inherent to the stimulation signal. Furthermore, [Figure 4.8](#) shows that the artifact component at f_{m2} is larger than or equal to the component at f_{m1} . In 52 EEG recordings, the artifact components at both modulating frequencies are statistically significant. Only in two such EEG recordings, the artifact at f_{m2} is smaller than at f_{m1} . In those cases, the difference is very close to zero (exact values are $-2.28 \cdot 10^{-4} \mu V$ and $-4.52 \cdot 10^{-4} \mu V$). Based on these observations, it can be concluded that the stimulation artifact increases with the modulation frequency due to the spectral nature of the stimulation signal. Furthermore, [\[21\]](#) found that EASSR amplitudes are lower at higher modulation frequencies as compared to the EASSR at 40 Hz. This implies that EASSRs might be more difficult to detect when evoked at higher modulation frequencies, since the EASSR-to-artifact ratio has decreased significantly. Examples of applications which rely on higher modulation frequencies - in the 80 Hz range - are the detection of EASSRs in infants and in individuals during sleep or anesthesia. [\[38, 21\]](#).

The stimulation artifact at both modulation frequencies increases approximately linearly with the stimulation level. With increasing distance to the stimulation electrode, the stimulation artifact at the modulation frequencies decays exponentially with similar decay rates. This decay is consistent with the smaller artifact amplitudes which are observed in contralateral channels as opposed to ipsilateral channels. [\[16\]](#) The overall signal strength, characterized by the RMS-value, exhibits similar scaling as a function of stimulation level and distance.

In the context of the second statement, [Figure 4.9](#) shows the normalized pulse asymmetry increases in absolute value with distance to the stimulation electrode according to an exponential relationship. This indicates the asymmetry-inducing

element in the system might be in its propagation. It decreases in absolute value with stimulation level in a nonlinear fashion which differs depending on the distance to the stimulation electrode. Furthermore, EEG recordings with a larger mean normalized pulse asymmetry also show a smaller amplitude difference between the artifact component at f_{m2} and f_{m1} . However, this relationship should be interpreted with caution as the pulse asymmetry is largest when the stimulation artifacts have the smallest amplitudes due to the exponential signal decay. Consequently, the pulse asymmetry cannot be related to the artifact amplitudes.

With respect to the third statement, the effects of nonlinearities in the system on the stimulation artifacts at the modulation frequencies seem limited due to the clear linear relationship between this artifact component and the stimulation level.

4.5 Conclusion

This chapter has analyzed the stimulation artifact from an experimental point of view in order to verify the statements presented in [Section 3.5](#).

With regards to the first statement, the experimental analysis has shown the stimulation artifact at the modulation frequency is consistently present across stimulation levels and recording electrodes. The magnitude of this artifact increases with the modulation frequency. The artifactual stimulation pulses in the EEG recordings show a flat profile. These observations indicate the stimulation signal model which takes the practical limitations into account is a more accurate model.

In the context of the second statement, the artifact EEG recordings display a pulse asymmetry. Aside from a constant DC offset, this pulse asymmetry shows a predominantly linear scaling with some nonlinear involvement. The mean normalized pulse asymmetry increases in absolute value over distance, indicating that the artifact propagation contributes to the observed asymmetry. As the signal decays over distance, no clear relationship between the artifact magnitudes and the pulse asymmetry can be observed.

With respect to the third statement, second and third order nonlinearities are clearly present in the system. However, in accordance with the theoretical analysis, their effect on the stimulation artifact at the modulation frequency is limited.

The subsequent three chapters will study how the results from the theoretical and experimental artifact characterization can be leveraged in artifact suppression methods.

Chapter 5

Artifact Suppression Methods

5.1 Introduction

Building upon the theoretical artifact analysis in [Chapter 3](#) and the experimental results in [Chapter 4](#), this chapter introduces methods for artifact suppression, enabling the detection of an EASSR and its characteristics in EEG recordings of CI recipients.

First, [Section 5.2](#) considers the dataset on which the developed methods are evaluated. Subsequently, [Section 5.3](#) outlines the evaluation methodology. Then, [Section 5.4](#) considers response models. The application of such response models to the EEG recordings without modeling the artifact results in a baseline performance. The three subsequent sections discuss artifact suppression methods developed in the context of this thesis, each containing both a response and an artifact model. Any improvement in the detection performance with respect to the established baseline performance can then be attributed to the explicit modeling of the artifact in these methods.

[Section 5.5](#) introduces the first method which exploits the known temporal characteristics of the EASSR and the stimulation artifact in order to separate them in an EEG recording. This method can be interpreted as an alternative approach to the Kalman filter model as discussed in [Section 2.6](#) such that regularization can be included more easily in the model estimation. [Section 5.6](#) introduces a novel method which attempts to tackle the fundamental causes of the stimulation artifact at the modulation frequency: the inherent component of the stimulation signal and the observed pulse asymmetry. [Section 5.7](#) discusses a third and final method, which extends the existing system identification method as discussed in [Section 2.6](#), by incorporating nonlinearities into the artifact model.

The general structure of each method presented in this chapter follows the high-level overview shown in [Figure 5.1](#) and contains both an artifact and response model branch. The prior knowledge about the artifact and response is incorporated in the input signals and model structures of their respective branch, which result in an estimated artifact and response. The parameters of both model branches are estimated by fitting the sum of the estimated artifact and response to the preprocessed

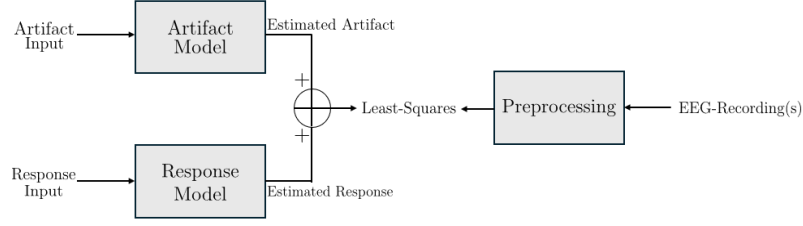


FIGURE 5.1: The general structure of all artifact suppression algorithms in this chapter, consisting of an artifact and response model. The structure and figure are based on [39, 40].

EEG recording(s) using a least-squares criterion, possibly including some form of regularization. The characteristics of the estimated response are compared to the noise level in order to determine whether or not a response is present.

Continuing upon the work presented in [40], the methods developed within this thesis apply an ordinary least-squares (OLS) to estimate the parameters of the artifact and response models. The OLS criterion only results in the maximum likelihood estimator (MLE) in a temporally uncorrelated noise regime. Since in EEG recordings, the noise consists of neural background activity, which does exhibit temporal correlations, the estimations resulting from OLS are no longer the MLE. Note that similar remarks can be made for the application of Kalman filters in this context. [14, 34] OLS can however still result in reasonable estimators as it minimizes the least squares error, and has shown its capabilities to achieve a separation of artifact and EASSR [40]. Since no noise recordings are available in the dataset, procedures such as prewhitening which incorporate knowledge of the noise statistics have not been explored. [4]

5.2 Dataset

The methods developed in this chapter are evaluated on an available dataset consisting of EEG recordings of 16 adult, unilateral CI recipients. All CIs are devices of manufacturer Cochlear Ltd. The EASSR stimulation signal is a train of symmetric, biphasic, cathodic-first pulses, which are amplitude-modulated with a sinusoidal signal oscillating at a single modulation frequency. The pulse width equals $25\ \mu s$ or $37\ \mu s$, depending on the recipient's stimulation settings, and an interphase gap of $8\ \mu s$. Custom software is used to generate these stimuli, which are directly delivered to the CI by means of the NIC4 research interface platform (Cochlear Ltd.). [40] The pulses are presented at a pulse rate of $900\ pps$ in monopolar (MP) stimulation mode, between an extracochlear electrode and intracochlear electrode 15 [40]. These stimulation settings are thus in correspondence with those for which the algorithms should be effective as mentioned in Section 2.6.

Due to the absence of ground truth characteristics of the EASSR, the evaluation of the methods relies on discriminatory properties between the EASSR and the artifact. As mentioned in Section 2.5, the group delay or latency is such a property. The

stimulation artifact propagates almost instantaneously, whereas the processing in the human brain results in a delay of about 40 *ms* for modulation frequencies in the 40 Hz range. [38] In order to exploit this discriminatory feature for evaluation purposes, three EEG recordings at distinct modulation frequencies (37 Hz, 40 Hz, and 43 Hz) are available for each CI-recipient. Inspection of the estimated EASSR phases at these frequencies allow to determine the group delay or latency of the estimated response. [38]

This thesis considers the EEG recordings at comfortable level and at subthreshold level to validate that the developed methods are capable of detecting the absence or presence of an EASSR. For 12 out of 16 subjects presented in [40], EEG recordings at both stimulation levels are available. Information about these subjects can be found in Table I, Subject Summary as presented in [40]. Four subjects, not mentioned in [40], but whose EEG recordings are available at both stimulation levels are included in this thesis.

5.3 Evaluation

As shown in Figure 5.1, each method presented in the subsequent sections results in an estimated response at each modulation frequency. The characteristics of these estimated responses are used to determine the presence or absence of an EASSR and its characteristics. The evaluation procedure described in this section is based on [40]. The selection of hyperparameter values is discussed thereafter.

First, for each modulation frequency, the amplitude and phase of the estimated response are compared to the variance over all epochs using a one-sample Hotelling T^2 test. [38] In this thesis, a significance value of five percent is used. In case the estimated response characteristics exceed this significance level, it is considered noise. Such a non-significant result is thus indicative that no EASSR is present. The results are only shown in Chapter 6 when the estimated response in an EEG channel is statistically significant at each modulation frequency. In those cases, the latency L can be calculated by a linear regression of the unwrapped phases [45]:

$$L = \left| -\frac{d\theta}{d\omega} \right| = \left| -\frac{1}{2\pi} \frac{d\theta}{df} \right| = \left| -\frac{a}{360^\circ} \right| \quad (5.1)$$

in which L represents the latency in seconds, θ the phase expressed in radians, ω the angular frequency, and a the slope expressed in degrees per Hz resulting from the linear regression of the estimated EASSR phases versus frequency. Similar to in [40], the estimated latencies of different methods are compared for the reference electrode *Cz* using a Kruskal-Wallis test, followed by a Dunn's test for multiple comparisons in case of statistical significance.

When the latency determined on the estimated response is indeed an EASSR, the latency is expected to be in the range of 35 to 55 ms. In case it is artifact-dominated, the latency is expected to be close to zero. The ideal EASSR detection method thus results in zero EASSR detections at the subthreshold stimulation level and a

5. ARTIFACT SUPPRESSION METHODS

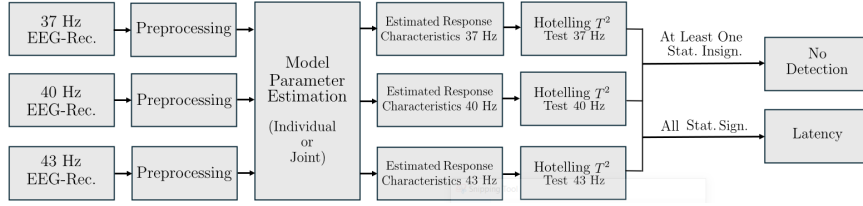


FIGURE 5.2: Visualization of the evaluation procedure. This evaluation framework is taken from [40].

detection with an estimated latency in the expected range for every EEG recording at comfortable level. [40] In order to achieve a separation in EASSR and artifact, the parameters of the response and artifact model are estimated using the EEG recordings at three modulation frequencies at a single stimulation level of a CI-recipient. Depending on the method, these three EEG recordings are processed jointly or individually. The estimated parameters then determine whether or not an EASSR is detected in each EEG recording, and what its characteristics are.

The EEG recordings at comfortable level are assumed to evoke an EASSR, while those at subthreshold level do not. This ground truth of whether an EASSR is expected in an EEG recording is never used in the model creation or parameter estimation. However, the false positive detection rate and the determined characteristics guide the tuning of hyperparameters, which might introduce an overfitting of the hyperparameter values on the current data resulting in poor performance on unseen data. Therefore, the available dataset is split into a validation and test set. The tuning of the hyperparameters is based on the validation set. Six out of sixteen are selected to be in the validation set before any validation had been done and such that they were representative for the data as based on pulse width and stimulation range. All results shown in this thesis are for the ten subjects of the test set. The evaluation procedure is visualized in Figure 5.2.

5.4 Baseline: No Artifact Suppression

To correctly evaluate the developed artifact suppression methods, a baseline detection performance has to be established. In some CI recipients, the stimulation artifact in contralateral channels has decayed to the extent that the EASSR can be directly detected at the modulation frequency without applying any form of artifact suppression. Furthermore, two methods presented in this thesis mask the stimulation pulses, which is assumed to further attenuate the stimulation artifact. In such cases, the EASSR detection should be attributed to the weak presence of the stimulation artifact rather than to the artifact suppression method.

This section establishes a baseline detection performance by only applying a response model to the EEG recordings; similar to in [14, 17, 15]. As discussed in Section 5.2, three EEG recordings are available of each subject at two different stimulation levels. These three EEG recordings can be processed either individually or jointly at a single

stimulation level for each CI recipient. The next two subsections discuss the response model for both cases. The last subsection discusses the masking operation.

5.4.1 Individual Evaluation

When the EEG recordings are analyzed individually, the response $\mathbf{r}^{f_m}$ due to stimulation at a modulation frequency f_m is estimated based on a single EEG recording, without incorporating information from the EEG recordings at the other modulation frequencies. The response model consists of a linear combination of a cosine $\mathbf{c}^{f_m}$ and a sinusoid $\mathbf{s}^{f_m}$, each oscillating at that modulation frequency f_m , with constant coefficients $\mathbf{b}_{resp} \in \mathbb{R}^2$:

$$\mathbf{r}^{f_m} = \begin{bmatrix} \mathbf{c}^{f_m} & \mathbf{s}^{f_m} \end{bmatrix} \cdot \mathbf{b}_{resp} \triangleq R^{f_m} \cdot \mathbf{b}_{resp} \quad (5.2)$$

The symbols in bold are column vectors and defined as:

$$\mathbf{c}^{f_m}[k] = \cos(2\pi f_m k T_s) \quad (5.3)$$

$$\mathbf{s}^{f_m}[k] = \sin(2\pi f_m k T_s) \quad (5.4)$$

$$\mathbf{c}^{f_m} = \begin{bmatrix} \mathbf{c}^{f_m}[0] & \mathbf{c}^{f_m}[1] & \dots & \mathbf{c}^{f_m}[K-1] \end{bmatrix}^T \quad (5.5)$$

$$\mathbf{s}^{f_m} = \begin{bmatrix} \mathbf{s}^{f_m}[0] & \mathbf{s}^{f_m}[1] & \dots & \mathbf{s}^{f_m}[K-1] \end{bmatrix}^T \quad (5.6)$$

in which k is the discrete time index, T_s the sampling period of the measured EEG recording, and K the total number of samples of the signal. The constant coefficients $\mathbf{b}_{resp}$ are determined through minimizing the least-squares cost J^{f_m} between the measured EEG recording $\mathbf{z}^{f_m}$ and the estimated response $\mathbf{r}^{f_m}$:

$$\mathbf{b}_{resp} = \arg \min_{\mathbf{b}_{resp} \in \mathbb{R}^2} J^{f_m} = \arg \min_{\mathbf{b}_{resp} \in \mathbb{R}^2} \|\mathbf{z}^{f_m} - \mathbf{r}^{f_m}\|_2^2 \quad (5.7)$$

The estimated EASSR amplitude $A_{EASSR}^{f_m}$ and phase $\theta_{EASSR}^{f_m}$ are determined as:

$$\begin{aligned} A_{EASSR}^{f_m} &= \|\mathbf{b}_{resp}\|_2 \\ \theta_{EASSR}^{f_m} &= \arctan\left(\frac{\mathbf{b}_{resp}[1]}{\mathbf{b}_{resp}[2]}\right) \cdot \frac{180^\circ}{\pi} \end{aligned} \quad (5.8)$$

Note that this response model essentially boils down to performing a Fourier transform on the measured EEG recording.

5.4.2 Joint Evaluation

The three EEG recordings at a single stimulation level can also be analyzed jointly using a response model introduced and presented in [40]. This approach models the response at each modulation frequency $f_{m,j}$ as the result of a filtering operation of a cosine $\mathbf{c}^{f_{m,j}}$ oscillating at that modulation frequency by a FIR system characterized the FIR-coefficients $\mathbf{b}_{resp} \in \mathbb{R}^{N_1+1}$:

$$\mathbf{r}^{f_{m,j}}[k] = \begin{bmatrix} \mathbf{c}^{f_{m,j}}[k] & \mathbf{c}^{f_{m,j}}[k-1q] & \dots & \mathbf{c}^{f_{m,j}}[k-N_1q] \end{bmatrix} \mathbf{b}_{resp} \quad (5.9)$$

in which $c^{f_{m,j}}$ is defined in Equation 5.3 and N_1 represents the order of the FIR-filter; The same FIR-coefficients $\mathbf{b}_{resp}$ are used to model the response at each $f_{m,j}$:

$$\begin{bmatrix} \mathbf{r}^{f_{m,1}} \\ \mathbf{r}^{f_{m,2}} \\ \mathbf{r}^{f_{m,3}} \end{bmatrix} = \begin{bmatrix} \mathbf{C}^{f_{m,1}} \\ \mathbf{C}^{f_{m,2}} \\ \mathbf{C}^{f_{m,3}} \end{bmatrix} \cdot \mathbf{b}_{resp} \quad (5.10)$$

where $\mathbf{C}^{f_{m,j}}$ represents a filter matrix defined as:

$$\mathbf{C}^{f_{m,j}} = \begin{bmatrix} c^{f_{m,j}}[N_1q] & c^{f_{m,j}}[(N_1-1)q] & \dots & c^{f_{m,j}}[0] \\ c^{f_{m,j}}[N_1q+1] & c^{f_{m,j}}[(N_1-1)q+1] & \dots & c^{f_{m,j}}[1] \\ \vdots & \vdots & \vdots & \vdots \\ c^{f_{m,j}}[K-1] & c^{f_{m,j}}[K-1-q] & \dots & c^{f_{m,j}}[K-1-N_1q] \end{bmatrix} \quad (5.11)$$

The sharing of these FIR-coefficients allows to integrate information from all three EEG recordings into the response model, in contrast to the individual model presented in Subsection 5.4.1. As the sampling frequency of the EEG recordings in the dataset is 262144 Hz, [40] sets the shift factor q to 4192 samples such that the coefficients of the response model result in a latency of about 0 ms, 16 ms, 32 ms, 48 ms, 63 ms, and 80 ms respectively. Furthermore, [40] sets N_1 to 5, such that the number of FIR-coefficients equals its maximal value of two times the number of modulation frequencies. These FIR-coefficients are determined through the minimization of a least-squares cost J over all modulation frequencies:

$$\mathbf{b}_{resp} = \arg \min_{\mathbf{b}_{resp} \in \mathbb{R}^{N_1+1}} J = \arg \min_{\mathbf{b}_{resp} \in \mathbb{R}^{N_1+1}} \sum_{f_{m,j}} \|(\mathbf{z}^{f_{m,j}} - \mathbf{r}^{f_{m,j}})\|_2^2 \quad (5.12)$$

The resulting coefficients $\mathbf{b}_{resp}$ are then transformed to their frequency domain representation $\mathbf{B}_{resp}(f)$ [40, 39]:

$$\mathbf{B}_{resp}(f) = \begin{bmatrix} 1 & \exp(-j2\pi qf/f_s) & \exp(-j4\pi qf/f_s) & \dots & \exp(-j2N_1\pi qf/f_s) \end{bmatrix} \cdot \mathbf{b}_{resp} \quad (5.13)$$

The amplitude $A_{EASSR}^{f_{m,j}}$ and phase $\theta_{EASSR}^{f_{m,j}}$ of each EASSR $\mathbf{r}^{f_{m,j}}$ are determined as:

$$\begin{aligned} A_{EASSR}^{f_{m,j}} &= \|\mathbf{B}_{resp}(f_{m,j})\|_2 \\ \theta_{EASSR}^{f_{m,j}} &= \angle \mathbf{B}_{resp}(f_{m,j}) \end{aligned} \quad (5.14)$$

5.4.3 Applying a skipping mask

The first and third method described in this chapter mask the stimulation pulses, since the model tends to overfit on them due to their large amplitude and therefore strong influence on the least-squares cost. This results in a bad artifact modeling in the interpulse interval. The masking of the stimulation pulses is introduced and presented in [40]. The skipping mask $\mathbf{m} \in \mathbb{R}^K$ is zero from 100 ms before to 450 ms after the start of each stimulation pulse, and one elsewhere. This mask is multiplied with the measured EEG recording(s) $\mathbf{z}^{f_m}$ prior to the analysis; the model parameters are then estimated on the non-masked samples.

5.5 Method 1: Time-Domain Artifact Suppression

The first method aims to exploit the known characteristics of the stimulation artifact in the time domain to separate this artifact from the EASSR. [Figure 2.6](#) displays the stimulation artifact. The dominant characteristics of this artifact are the biphasic, cathodic-first stimulation pulses and the exponentially decaying tail in the interpulse intervals. [\[40, 16\]](#) In an initial approach, the stimulation pulses are masked and an exponentially decaying tail is fitted to each interpulse interval individually and subsequently subtracted. The reasoning behind this initial method is that the masking of the stimulation pulses in conjunction with the removal of the typical artifact tail would ease the detection of EASSRs in subsequent processing steps. However, preliminary results show that the removal of the exponentially decaying tail on a pulse-to-pulse basis also results in the suppression of the EASSR. Furthermore, the relatively low SNR of the EEG recordings results in a poor estimation of the exponentially decaying tails due to the limited data in each interpulse interval.

Therefore, another approach is taken by simultaneously fitting the exponentially decaying tail and other artifact components with a response model to the observed EEG recording. In that perspective, this approach is very similar to the Kalman filter (KF) based method introduced in [\[34\]](#) and further extended in [\[14\]](#).

In these approaches, the artifact at each time point is modeled using a number of predetermined artifact templates. The contribution of each artifact template is determined through applying a Kalman filter to the EEG recording. [\[14\]](#) uses four artifact templates: a monophasic stimulation pulse, an exponentially decaying tail - both modulated and unmodulated -, and a constant bias. The response is modeled as the linear combination of a cosine and sinusoid oscillating at the modulation frequency, as discussed in [Subsection 5.4.1](#).

In this thesis, a similar approach is taken. The stimulation pulses in the EEG recording to analyze are masked, such that only the interpulse intervals are being analyzed. In each interpulse interval, the different artifact templates are fitted to the observed EEG data together with a response model using a least-squares criterion. The masking of the stimulation artifact renders the first artifact template of [\[14\]](#) - a monophasic stimulation pulse - unnecessary. The second - the exponentially decaying tail - and last - the constant bias - templates of [\[14\]](#) are also included in the model. These templates are represented as:

$$\mathbf{a}_{exp} = \begin{bmatrix} a_{exp}[1] \\ a_{exp}[2] \\ \vdots \\ a_{exp}[N] \end{bmatrix} \quad \mathbf{a}_{bias} = \begin{bmatrix} 1 \\ 1 \\ \vdots \\ 1 \end{bmatrix} \quad (5.15)$$

in which $a_{exp}[k] = \exp(-\alpha k T_s)$ represents the k -th sample index of the artifact template representing the exponentially decaying tail. The estimation of α is considered in a subsequent section. $\mathbf{a}_{bias}$ reflects the template for the bias. The length of the vectors, N , equals the number of samples in the interpulse interval.

The artifact model can thus be written as:

$$A_{exp} = \text{blockdiag}(\mathbf{a}_{exp}, \dots, \mathbf{a}_{exp}) \quad A_{bias} = \text{blockdiag}(\mathbf{a}_{bias}, \dots, \mathbf{a}_{bias}) \quad (5.16)$$

in which the number of repetitions equals the number of interpulse intervals of the EEG recording.

In this method, the EEG recordings are analyzed individually. This results in the following signal model for the analysis of an EEG recording at the modulation frequency f_m :

$$\mathbf{s}_{est}^{f_m} = \begin{bmatrix} A_{exp} & A_{bias} & R^{f_m} \end{bmatrix} \cdot \begin{bmatrix} \mathbf{b}_{exp} \\ \mathbf{b}_{bias} \\ \mathbf{b}_{resp} \end{bmatrix} \quad (5.17)$$

All signal model parameters are then estimated by minimizing a least-squares cost function, including regularization terms:

$$J = \|\mathbf{z}^{f_m} - \mathbf{s}_{est}^{f_m}\|_2^2 + \beta \cdot \|\Gamma \mathbf{b}_{exp}\|_2^2 + \gamma \cdot \|\Gamma \mathbf{b}_{bias}\|_2^2 + \lambda \cdot \|\mathbf{b}_{resp}\|_2^2 \quad (5.18)$$

in which Γ represents a Tikhonov regularization matrix penalizing the second order derivative. The hyperparameters are selected as $\beta = 5$, $\gamma = 500$ and $\lambda = 100$ based on results on the validation set. The regularization reduces the effective number of parameters and ensures that the artifact templates cannot vary too much from interval to interval. This is especially important for the bias term which is included to capture slow variations of the DC-components in each interval.

As in [14], the estimation of the exponential decay factor α is performed on the average interpulse interval of the EEG recording. An initial estimate of α is obtained through a linear regression on the logarithm of the exponential tail, and further refined through a non-linear least squares which includes a bias-term in the estimation. The estimated decay factor is then used in the template.

5.6 Method 2: Pulse Averaging

A second method focuses on the underlying causes for the stimulation artifact at the modulation frequency f_m . The theoretical analysis in [Chapter 3](#) shows that the stimulation signal inherently contains a spectral component at the modulation frequency f_m . Subsequent analyses show that this inherent component is further magnified by nonidealities such as a pulse asymmetry or nonlinearities.

This second method aims to suppress the inherent component and the observed pulse asymmetry by computing the average of each measured pulse. This operation essentially integrates the signal over a pulse period, and normalizes it to the duration of the pulse. The resulting signal of pulse averages can be described as:

$$v(p) = \frac{\int_{p \cdot T_c + T_{shift}}^{(p+n) \cdot T_c + T_{shift}} z(t) dt}{n \cdot T_c} \quad (5.19)$$

in which p represents the pulse index, T_c the pulse period, $\bar{z}$, and $z(t)$ the mean epoch of the EEG signal. The parameter n describes the number of pulses over which the averaging is performed, and is initially set to one. The parameter T_{shift} allows to shift the time window over which the averaging is performed, and is selected such that the averaging starts 100 ms before to the start of each pulse. In this manner, effects prior to the stimulation pulses are included in the overall average of that pulse. The pulse averaged signal $v(p)$ is then analyzed by applying a response model to it, either individually or jointly. In the high-level overview of Figure 5.1, no artifact model branch is present as the artifact suppression is included in the preprocessing of the EEG recording.

The averaging of each pulse exploits the different nature of the EASSR and the stimulation artifact.

5.6.1 Effect on the EASSR

To study the effect of pulse averaging on the response, the EASSR is modeled as a sinusoidal signal oscillating at the modulation frequency f_m . Note that this frequency is typically small in comparison to the stimulation rate f_c as stated in Section 2.4, such that pulse averaging essentially downsamples the EASSR signal.

Figure 5.3 illustrates the effect of pulse averaging on the response signal. The left subfigure shows a zoom of a sinusoidal signal of 40 Hz modeling the response; the dashed lines indicate the pulse durations. The middle subfigure shows the same simulated response over a larger time window, and reveals the slow oscillatory behavior in comparison to the pulse duration. The circles in the right subfigure show the downsampling effect of pulse averaging on this simulated response signal. This demonstrates that the pulse averaging operation preserves the sinusoidal oscillations of the EASSR.

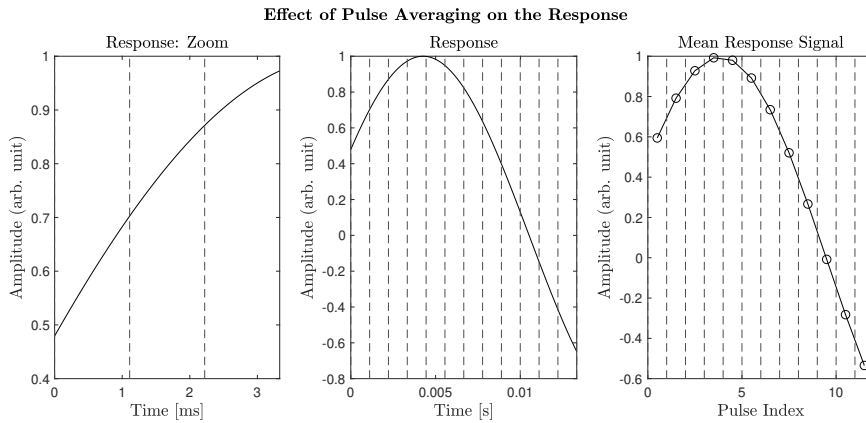


FIGURE 5.3: Effect of the pulse averaging method on the simulated EASSR

5.6.2 Effect on the Stimulation Artifact

Since the stimulation signal has to be charge-balanced to avoid tissue damage [51], the mean of each pulse is equal to zero in the ideal case. In practice, however, this will not be the case due to three reasons. First, according to [28], "the nonideal nature of stimulator electronics means that perfect charge balance is impossible to achieve" [28]. Second, Chapter 4 has shown that the pulses exhibit asymmetric features in the EEG recordings, resulting in a nonzero mean of each observed pulse. Third, the temporal extent of the stimulation pulses is increased due to the anti-aliasing low-pass filter and the system characteristics. This last effect results in exponentially decaying tails, which exceed the interpulse interval in case of a stimulation rate of 900 Hz and in MP mode stimulation. [44, 16]. Despite these nonidealities, the inherent component is removed and the nonideal and nonlinear contributions to the stimulation artifact are attenuated by the averaging procedure.

Figure 5.4 illustrates the effect of pulse averaging on the stimulation artifact. This signal is measured at the third and referenced to the last electrode in the experimental set-up as described in Section 4.2. The stimulation level is 255 CLs with a modulation depth of 50 CLs and a single modulation frequency of 37 Hz. The left subfigure shows a zoom of the observed artifacts in the EEG recording. The middle subfigure shows the same signal over a larger temporal extent. The right subfigure shows the effect of the averaging operation on the artifact; note the scale difference of the y-axis. It is

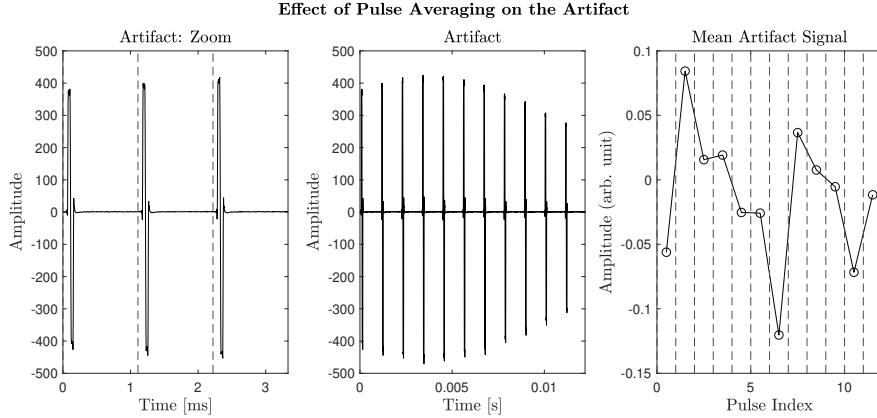


FIGURE 5.4: Effect of the pulse averaging method on the stimulation artifact

especially of interest whether pulse averaging reduces the spectral component at the modulation frequency. Table 5.1 shows the spectral component at the modulation frequency before and after the averaging operation on the described signal over the various stimulation electrodes, at maximal stimulation level. A clear reduction is observed, which is more pronounced at electrodes closer to the stimulation electrodes.

TABLE 5.1: Effect of pulse averaging on the observed stimulation artifact at the modulation frequency over distance. Stimulation level of 255 CLs, modulation depth and frequency of 50 CLs and 37 Hz respectively.

Electrode Number	1	2	3	4	5	6
$G(f_m)$	0.215	0.123	0.068	0.049	0.034	0.035
$G_{averaged}(f_m)$	0.072	0.036	0.021	0.021	0.024	0.032

5.6.3 Considerations and Extensions

Similar to the pulse asymmetry measure as discussed in [Chapter 4](#), pulse averaging produces a single measure from each pulse. It essentially downsamples the signal which can potentially induce aliasing. Since the pulse averaging in itself has a low-pass characteristic, aliasing is not expected to pose a problem. Results on the validation set confirm that low-pass filtering prior to pulse averaging does not alter the results.

An extension to the pulse averaging approach involves averaging over multiple pulses; which corresponds to setting the parameter n to an integer value larger than one. Since the exponentially decaying tail exceeds the interpulse interval, this extension might further reduce the artifact component at the modulation frequency. The EASSR is expected not to be affected as long as the Nyquist criterion is satisfied. For a pulse rate of 900 *pps*, n can be increased to 10 such that frequencies up to 45 Hz can still be represented. Results on the validation set show that the estimated latencies decrease with averaging over an increasing number of subsequent pulses. Therefore, this extension is not further explored.

Since this method suppresses the artifact by processing the measured EEG recording individually, no benefit is expected in processing the EEG recordings at different modulation frequencies jointly. Results on the validation set show no performance increase in using the joint response model.

5.7 Method 3: Nonlinear System Identification

A third method extends the linear system identification approach introduced and discussed in [\[40\]](#). [Subsection 5.7.1](#) outlines the specifics of this linear approach and is based on [\[40\]](#). Subsequently, [Subsection 5.7.2](#) introduces an extension to this method which incorporates nonlinearities into the model’s artifact branch.

5.7.1 Linear System Identification

The model presented in this subsection is introduced and presented in [\[40\]](#). This subsection provides an overview of this model. The next subsection discusses the nonlinear extension of this model. Using the linear system identification approach, the estimated artifact $\mathbf{a}^{f_m}$ is the result of a filtering operation of an input $\mathbf{u}^{f_m}$ by a

FIR-system characterized by FIR-coefficients $\mathbf{b}_{\text{arti}} \in \mathbb{R}^{N_2+1}$:

$$a^{f_m}[k] = \begin{bmatrix} u^{f_m}[k] & u^{f_m}[k-1] & \dots & u^{f_m}[k-N_2] \end{bmatrix} \cdot \mathbf{b}_{\text{arti}} \quad (5.20)$$

in which N_2 represents the order of the FIR-system. The input signal u^{f_m} is modeled as a Dirac delta pulse train, modulated by a sinusoidal signal with the same amplitude and modulation depth as used in the stimulation.

The FIR-coefficients $\mathbf{b}_{\text{arti}}$ of this artifact model are estimated simultaneously with those of the response model $\mathbf{b}_{\text{resp}}$ using all three EEG recordings jointly. The three EEG recordings z^{f_m} , obtained at three distinct modulation frequencies f_m , are stacked into a single vector $\mathbf{z}$. A joint response filter matrix $\mathbf{C}^{f_m}$ is obtained as presented in Equation 5.9. The artifact filter matrix $\mathbf{U}^{f_m}$ is obtained by vertically stacking the row vector in Equation 5.20 for time indices from 0 to $K-1$. This results in a final model in which the response and artifact are modeled simultaneously and jointly over all three modulation frequencies:

$$\underbrace{\begin{bmatrix} \mathbf{z}^{37} \\ \mathbf{z}^{40} \\ \mathbf{z}^{43} \end{bmatrix}}_{\mathbf{z}} = \underbrace{\begin{bmatrix} \mathbf{C}^{37} & \mathbf{U}^{37} \\ \mathbf{C}^{40} & \mathbf{U}^{40} \\ \mathbf{C}^{43} & \mathbf{U}^{43} \end{bmatrix}}_{\mathbf{H}} \cdot \underbrace{\begin{bmatrix} \mathbf{b}_{\text{resp}} \\ \mathbf{b}_{\text{arti}} \end{bmatrix}}_{\mathbf{x}} + \mathbf{v} \quad (5.21)$$

in which $\mathbf{v}$ represents a noise vector. Both the vector of measured EEG recordings, $\mathbf{z}$, and the columns of the matrix containing the regressors $\mathbf{H}$ are mean-centered. The stimulation pulses are masked in the measured EEG recordings vector $\mathbf{z}$ and only unmasked samples are used in the estimation of the unknown FIR-coefficients $\mathbf{x}$. The estimation is performed by minimizing the least squares cost function, in which a regularization term is included:

$$J = \|\mathbf{H}\mathbf{x} - \mathbf{z}\|_2^2 + \alpha \|\Gamma\mathbf{x}\|_2^2 \quad (5.22)$$

The matrix Γ is selected such that a Tikhonov regularization is applied to the FIR-coefficients of the response model $\mathbf{b}_{\text{resp}}$; no regularization is applied to the FIR-coefficients of the artifact model $\mathbf{b}_{\text{arti}}$.

The filter length N_1 of the response model is set to 5 as motivated earlier. The filter length N_2 of the artifact model is set to 375 in this implementation such that the artifact filter length exceeds the interpulse interval of approximately 290 samples. After applying the masking operation, the number of parameter reduces to 147 parameters.

In [40], the hyperparameter α is determined using the subthreshold recordings of all subjects and set to the balance of the lowest possible regularization and the lowest number of false positive detections. This procedure results in an optimal value for α of 5000.

5.7.2 Nonlinear System Identification

In this thesis, the linear approach system identification approach is extended such that second order nonlinearities are included in the model. The theoretical artifact

analysis shows these nonlinearities are able to contribute to the stimulation artifact at the modulation frequency. The experimental artifact analysis shows the system indeed exhibits a nonlinear behavior.

In order to include these second order nonlinear terms in the model, a Volterra series is selected. The linear artifact model presented in Equation 5.20 can be written as:

$$a^{f_m}[k] = \sum_{m=0}^{N_2} \mathbf{b}_{\text{arti}}[m] u^{f_m}[k-m] \quad (5.23)$$

A Volterra series extends this linear FIR model such that higher order nonlinear components are added [9]:

$$a[k] = \mathbf{b}_{\text{arti},0} + \sum_{n=1}^{\infty} \sum_{m_1=0}^{N_1} \dots \sum_{m_n=0}^{N_n} \mathbf{b}_{\text{arti},n}[m_1, \dots, m_n] u[k-m_1] \dots u[k-m_n] \quad (5.24)$$

Note that a Volterra series reduces to the linear FIR model for $n = 1$. In the context of obtaining an accurate artifact model for the spectral component at the modulation frequency f_m , the theoretical analysis has shown that only first and second order contributions are able to contribute significantly to the stimulation artifact at the modulation frequency. The third and higher order nonlinear contributions are negligible. To adequately model the stimulation artifact, the Volterra Series presented in Equation 5.24 can thus be truncated by omitting these higher order terms. Furthermore, since the observed EEG recordings $\mathbf{z}^{f_m}$ and the input signals $\mathbf{u}^{f_m}$ are mean-centered, the zeroth order term $\mathbf{b}_{\text{arti},0}$ equals zero:

$$a[k] = \sum_{m=0}^{N_2} \mathbf{b}_{\text{arti},1}[m] u[k-m] + \sum_{m_1=0}^{N_2} \sum_{m_2=0}^{N_2} \mathbf{b}_{\text{arti},2}[m_1, m_2] u[k-m_1] u[k-m_2] \quad (5.25)$$

Note that the parameters $\mathbf{b}_{\text{arti},2}[m_1, m_2]$ can still be estimated using an OLS with regularization terms since Equation 5.25 is still linear in its parameters, despite its capabilities to model second order nonlinearities.

The next subsection will study the relationship between the presented Volterra series and common nonlinear models such as a Taylor series, and Hammerstein and Wiener model structures [9]. Subsequently, the number of parameters is considered based on which an adequate input representation is selected.

Relationship to Common Nonlinear Models

By considering special cases of $\mathbf{b}_{\text{arti},n}[m_1, \dots, m_n]$, which is often referred to as the n -th order Volterra kernel [9, 19], in Equation 5.24, the Volterra Series can be related to common nonlinear model structures. The Volterra series reduces to a Taylor Series when the Volterra kernels are selected as [9]:

$$\mathbf{b}_{\text{arti},n}[m_1, \dots, m_n] = b_{\text{arti},n,\text{diag}} \delta_{m_1, \dots, m_n} \quad (5.26)$$

in which n ranges from 1 to infinity and $b_{arti,n,diag}$ is a constant value for each n . The symbol $\delta_{i,...,j}$ represents the Kronecker Delta function, which prevents samples at different time indices from exerting an influence on each other. The Volterra series can thus be interpreted as an extension to the Taylor series in which memory effects are included. This shows the Volterra series is able to include nonlinear dynamic effects, whereas the Taylor series is only able to model static nonlinearities. [9]

Other popular nonlinear model structures are the Wiener and Hammerstein model. A Wiener model consists of a linear dynamic system followed by a static nonlinearity. A Hammerstein model is the counterpart of the Wiener system and consists of a static nonlinearity, followed by a linear dynamic system. For polynomial static nonlinearities, these models reduce to special cases of a truncated Volterra Series. [9] Furthermore, a Wiener-Hammerstein model - which concatenates a Wiener and a Hammerstein model resulting in a single static nonlinearity between two linear dynamical systems - can also be represented by a truncated Volterra Series for polynomial nonlinearities. [9]

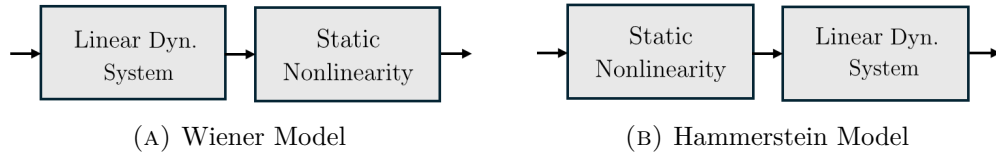


FIGURE 5.5: Structure of a Wiener and Hammerstein Model. Figure based on [9, 41]

The flexibility makes of the (truncated) Volterra Series a very appealing modeling approach. Furthermore, due to the linear dynamics and the lack of feedback, the (truncated) Volterra Series is guaranteed to be stable. [36]

Number of Parameters

However, these favorable properties come at a cost. From Equation 5.24, it is apparent that the Volterra series representation suffers from the curse of dimensionality. [36] Even a truncated Volterra Series which only includes the first and second order kernels result in a large amount of parameters. For instance, the artifact model uses a memory length N_2 of 375 samples such that interpulse interval and the interpulse behavior can be modeled. Brute-forcefully applying a truncated Volterra series in this case would thus result in a total of $N_2^2 + N_2 = 141\,000$ parameters to model the second order contributions. However, as $\mathbf{b}_{arti,2}[m_1, m_2] = \mathbf{b}_{arti,2}[m_2, m_1]$, the number of parameters is approximately halved. The masking of the stimulation pulses further reduces the number of parameters, but the number of parameters remains problematic.

A first solution to this problem can be found in regularizing the OLS problem such that the effective number of parameters is reduced. [43] However, due to the excessive amount of parameters, regularization won't suffice.

Input Representation

A suited selection of the input representation can result in a drastic reduction in the amount of parameters required to represent the second order Volterra kernel. In the original system identification method, a Dirac pulse train modulated by a sinusoidal signal constructed with the stimulation parameters is used. Such a Dirac train as input representation results in only a limited number of parameters in the second order Volterra kernel which are able to contribute since $u[k - m_1]u[k - m_2]$ is only nonzero in case:

$$|m_1 - m_2| = k \cdot f_s / f_c \quad (5.27)$$

in which f_s , f_c represent the sampling and carrier frequency respectively, and k a positive integer. This implies that the nonlinear branch of this model includes the square of the original input signal as well as multiplications between two subsequent Dirac pulses.

Another possibility is to use a modulated monophasic pulse train with the correct pulse duration. This representation allows the inclusion of the pulse duration into the model, which has been shown to have an effect on the stimulation artifact.

When the Dirac train input is selected, this results in an equal amount of parameters for the linear and nonlinear branches of the artifact model. After masking the stimulation pulses, both branches require 147 parameters, which can be reliably estimated using all three EEG recordings, containing about 277 700 samples each which represents about 1.024 seconds since the sampling rate equals 262144 Hz. The monophasic pulse as input results in about 1000 or 1500 parameters in the nonlinear model, for a pulse duration of 25 μs and 37 μs respectively.

The results on the validation set lead to the selection of the Dirac train representation as the input signal to the artifact model in the final extended model.

Chapter 6

Results

This chapter presents the results of the methods developed in this thesis. First, [Section 6.1](#) establishes a baseline detection performance by only applying a response model to the measured EEG recordings without any form of artifact suppression. Therefore, any improvement with respect to this baseline performance can be attributed to the developed artifact suppression method. Then, [Section 6.2](#) shows the results for the time domain artifact suppression method. Next, the results obtained using the pulse averaging are displayed in [Section 6.3](#). Lastly, [Section 6.4](#) shows the performance of the linear and nonlinear system identification (SI) approaches.

The results are displayed for the ten subjects in the test set, following to the methodology discussed in [Section 5.3](#). Three contralateral recordings and two ipsilateral recordings are available per subject, resulting in a total of 30 contralateral recordings and 20 ipsilateral recordings in the test set.

For the estimated EASSR latencies, all results are shown in the form of boxplots and are grouped based on stimulation level (subthreshold level and comfortable level) and on EEG electrode position (ipsilateral or contralateral EEG channels). Therefore, four figures are shown for each method. Each of these figures contains three boxplots, showing the influence of the reference channel. The labels on the x-axis indicate the reference electrode used in the analysis, with the number next to it indicating the number of statistically significant results for that reference electrode. Note that the latency is only shown when it could be determined based on three statistically significant response estimations, as explained in [Section 5.3](#). The ideal detection method thus displays zero results for both channels at subthreshold stimulation level. At comfortable level, it results in 30 contralateral and 20 ipsilateral EASSR detections. Typical EASSR latencies range from 35 *ms* to 55 *ms*, as indicated by the dashed horizontal lines in each figure. [\[40, 38\]](#)

For the estimated amplitudes, the results are only shown for the reference electrode *Cz* and displayed in a figure consisting of four subfigures. The upper two subfigures display results for EEG recordings at subthreshold stimulation level; the bottom two for those at comfortable stimulation level. The left and right two subfigures reflect performance in contra- and ipsilateral channels respectively.

6.1 Baseline: No Artifact Suppression

6.1.1 Latency

Figure 6.1 displays the estimated latencies when only a response model is applied to each EEG recording individually without masking the stimulation pulses. In contralateral EEG channels at subthreshold stimulation level, the number of false positive detections equals 9, 9, and 4 out of 30 results for the *Cz*, *Fz*, and *Fpz* as reference electrode respectively. In this chapter, the results are reported for the reference electrodes *Cz*, *Fz*, and *Fpz* and are always presented in that order. In ipsilateral EEG channels at this stimulation level, the number of false positive detections equals 16, 17, and 15 out of 20 results for the three reference electrodes respectively. At this stimulation level, all estimated latencies are relatively low and close to zero.

In contralateral EEG channels at comfortable stimulation level, 30, 28, and 28 out of 30 results are detected for the three reference electrodes respectively. The median latency is close to the lower bound of the expected range. In ipsilateral EEG channels at this stimulation level, 20, 19, and 19 results out of 20 are detected depending on the selected reference electrode. The median latency is below or close to the lower bound of the expected range. In comparison to contralateral channels, the estimated latencies in ipsilateral channels display a higher variance.

Figure 6.2 shows the latencies estimated by the same response model when the stimulation pulses are masked in the EEG recording. In contralateral EEG channels at subthreshold stimulation level, the number of false positive detections equals 7, 5, and 1 out of 30 results for the different reference electrodes. For each reference electrode, the number of false positives has decreased due to the masking of the stimulation pulses. In ipsilateral channels at this stimulation level, 16, 18, and 14 out of 20 recordings indicate a false positive result. The overall number of false positive results remains unchanged, while the estimated latencies show a smaller variance.

In contralateral EEG channels at comfortable stimulation level, 25, 22, and 18 out of 30 results are detected for the three reference channels respectively. For each reference electrode, the overall number of detections has decreased. The masking procedure results in a median latency in the middle of the expected range, alongside a large variance. In ipsilateral channels at this stimulation level, 20, 19, and 19 out of 20 results are detected. The median latency is low and close to zero.

Similar conclusions hold for the response model, introduced in **Subsection 5.4.2**, which analyzes the three EEG recordings at a single stimulation level jointly. For completeness, these results are included in **Appendix B**.

6.1.2 Amplitude

Figure 6.3 shows the amplitudes estimated by the individual response model without any form of artifact suppression for the reference electrode *Cz*. **Figure 6.3a** and

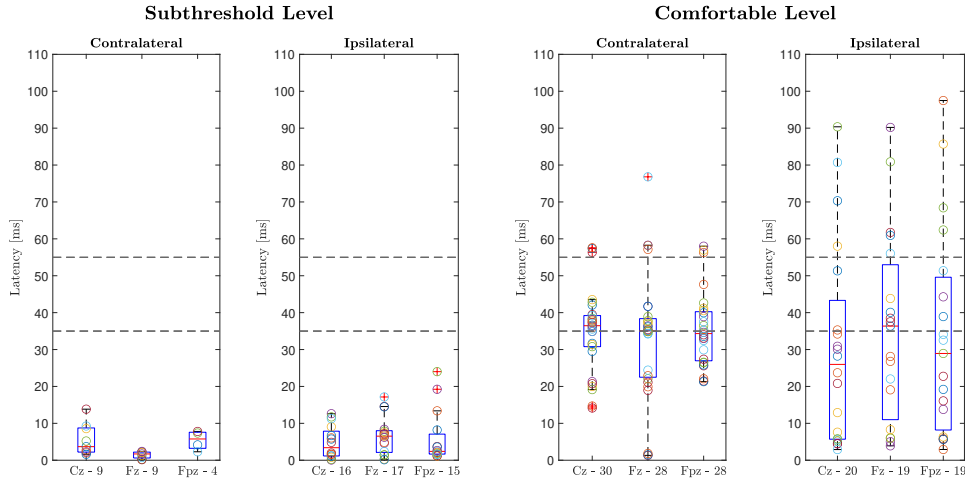


FIGURE 6.1: Latencies estimated by the response model without artifact suppression, individual processing

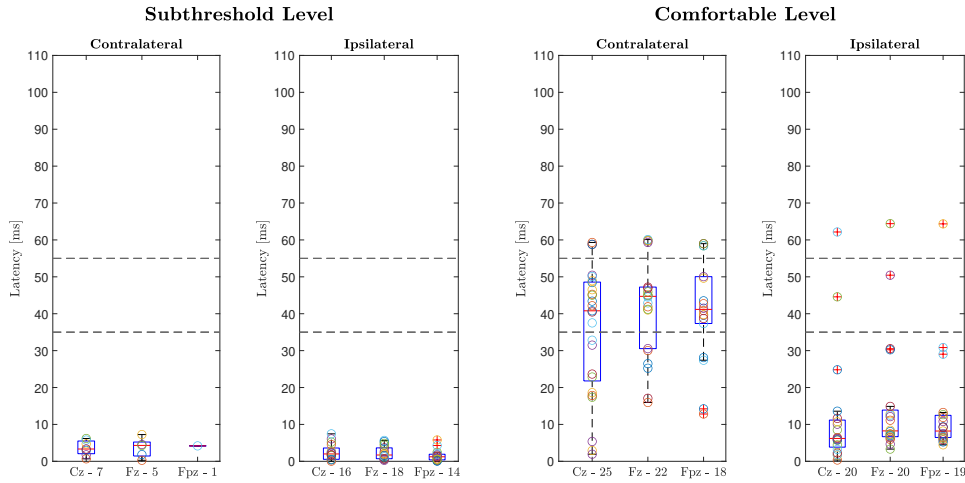
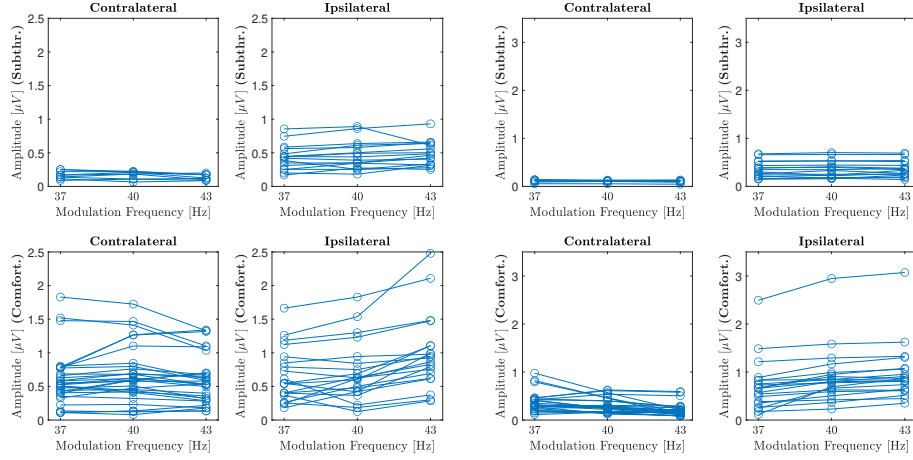


FIGURE 6.2: Latencies estimated by the response model without artifact suppression, individual processing, and masking of the stimulation pulses

Figure 6.3b show the results ex- and including the masking operation of the stimulation pulses. In each figure, the results for the subthreshold stimulation level are shown in the two upper subfigures, while the two lower subfigures show the results for stimulation at comfortable level. Note that the scale of the y-axis is different in both figures. In general, the estimated amplitudes are larger in ipsilateral channels as compared to contralateral channels. The masking operation results in a reduction of estimated amplitudes in contralateral channels while in ipsilateral channels, no amplitude reduction is observed; the estimated amplitudes in a single channel of a

subject are even amplified after the masking operation.



(A) Without masking the stimulation pulses (B) With masking the stimulation pulses

FIGURE 6.3: Amplitudes (for *Cz* as reference electrode) estimated by the response model without artifact suppression, individual processing. Subthreshold stimulation level (upper left and right) and comfortable stimulation level (bottom left and right) in each figure.

6.2 Method 1: Time-Domain Artifact Removal

6.2.1 Latency

Figure 6.4 shows the latencies as estimated by the time domain artifact suppression (TDAS) method. This method analyzes the EEG recordings at each modulation frequency individually and masks the stimulation pulses, the results should therefore be compared to Figure 6.2.

In contralateral EEG channels at subthreshold stimulation level, no false positives are detected in the 30 recordings, independent of the reference electrode. In ipsilateral EEG channels, the number of false positive detections equals 9, 9 and 8 out of 20 results. The estimated latency of these false positive detections is close to zero. In contrast to the baseline performance, the number of false positives is thus reduced to zero in contra- and approximately halved in ipsilateral EEG channels. No Kruskal-Wallis test could be conducted at subthreshold stimulation level due to the emptiness of a group.

In contralateral EEG channels at comfortable stimulation level, 22, 26, and 23 out of 30 results are detected. The median latency is in the center of the expected range. The results contain outliers below and above the expected range for all reference channels, but are most distinct for *Cz*. In ipsilateral channels at this stimulation level, 17, 18, and 18 out of 20 results are detected. The median latency is far below

the expected range. Between this method and the baseline without masking, a Kruskal-Wallis test found a significant difference among the four groups. Dunn's test found a significant difference in the means of TDAS-contra and response-indiv.-contra ($p = 0.012$), TDAS-contra and response-indiv-ipsi ($p = 0.0003$), TDAS-ipsi and response-indiv-contra ($p = 0.013$) and TDAS-ipsi and TDAS-contra ($p < 0.0001$). Between this method and the baseline with masking, a Kruskal-Wallis test found a significant difference among the four groups. Dunn's test found a significant difference in the means of: response-indiv.-contra and response-indiv-ipsi ($p < 0.0001$), TDAS-contra and response-indiv-ipsi ($p < 0.0001$), TDAS-ipsi and response-indiv-contra ($p = 0.04$) and TDAS-ipsi and TDAS-contra ($p = 0.001$).

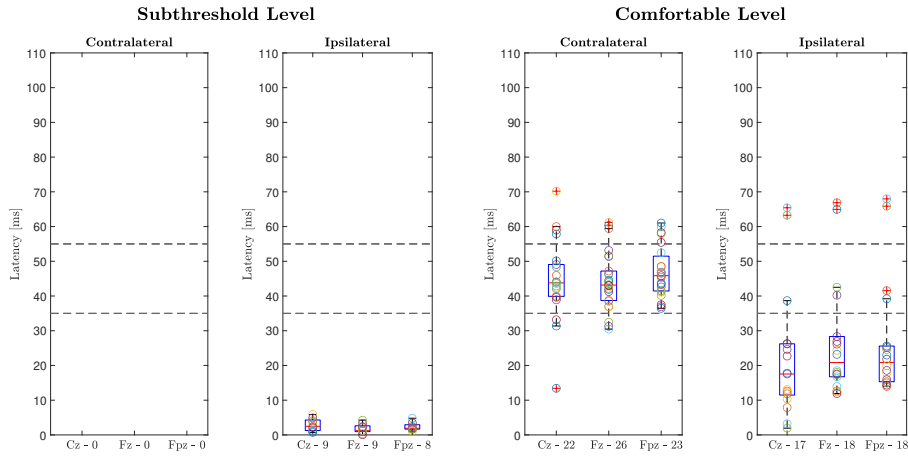


FIGURE 6.4: Latencies estimated by the time domain artifact suppression method.

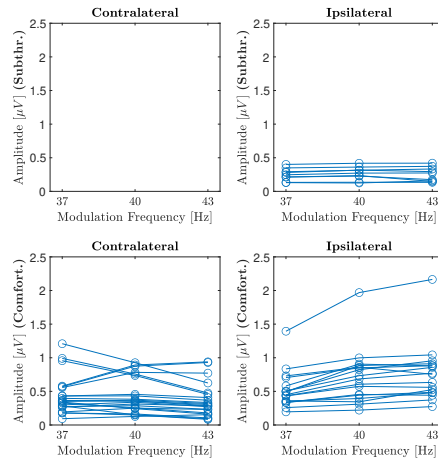


FIGURE 6.5: Amplitudes (for Cz as reference electrode estimated by the time domain artifact suppression method. Subthreshold (upper two subfigures) and comfortable stimulation level (bottom two subfigures)

6.2.2 Amplitude

Figure 6.5 displays the amplitudes estimated by the time domain artifact suppression method for reference electrode *Cz*. In contralateral EEG channels at comfortable level, the estimated amplitudes are similar to the baseline performance shown in Figure 6.3b. In ipsilateral EEG channels, the amplitudes are clearly smaller at subthreshold stimulation level. At comfortable level, all amplitudes are in a similar range as the baseline performance although the largest amplitudes are reduced.

6.3 Method 2: Pulse Averaging

6.3.1 Latency

Figure 6.6 shows the latencies estimated by the pulse averaging (PA) method with averaging over a single pulse. This method analyzes the EEG recordings at each modulation frequency individually without masking the stimulation pulses, the results should therefore be compared to the baseline of Figure 6.1.

In contralateral EEG channels at subthreshold stimulation mode, the number of false positives equals 3, 6, and 0 out of 30 results (in contrast to the baseline performance of 9, 9, 4). In ipsilateral EEG channels, 4, 6, and 2 out of 20 recordings resulted in a false positive detection (in contrast to the baseline performance of 16, 17, and 15). The estimated latencies are close to zero. The number of false positive detections is thus strongly reduced. Between this method and the baseline without masking, a Kruskal-Wallis test found no significant difference in the distributions of the groups ($p = 0.136$) at subthreshold level. In contralateral channels at comfortable stimulation level, 26, 28, and 28 out of 30 results are detected. The median latency of these estimated EASSRs are towards the middle of the expected range, although multiple estimated latencies are outside the expected range. In ipsilateral EEG channels at this stimulation level, 18, 19, and 18 out of 20 results are detected. The median latency varies around the upper bound of the expected range, depending on the reference electrode. The variance of the expected latencies is larger as compared to the results in contralateral channels. Between this method and the baseline without masking, a Kruskal-Wallis test found a significant difference in the distributions of the groups ($F(3, 90)$, $p < 0.00001$). Dunn's test finds a significant difference between PA-ipsi and response-indiv.-contra ($p < 0.0001$), PA-ipsi and response-indiv.ipsi ($p < 0.00001$), PA-contra and response-indiv.-ipsi ($p = 0.01$) and PA-contra and PA-ipsi ($p = 0.012$).

6.3.2 Amplitude

Figure 6.7 shows the amplitudes estimated by the pulse averaging method over a single pulse. In contralateral channels, the amplitudes are similar to the baseline, although the average amplitude is lower at comfortable stimulation level. Additionally, the estimated amplitudes in contralateral channels are similar as those obtained by

the time domain artifact suppression method. In ipsilateral channels, the amplitudes are lower than for the baseline at both stimulation levels.

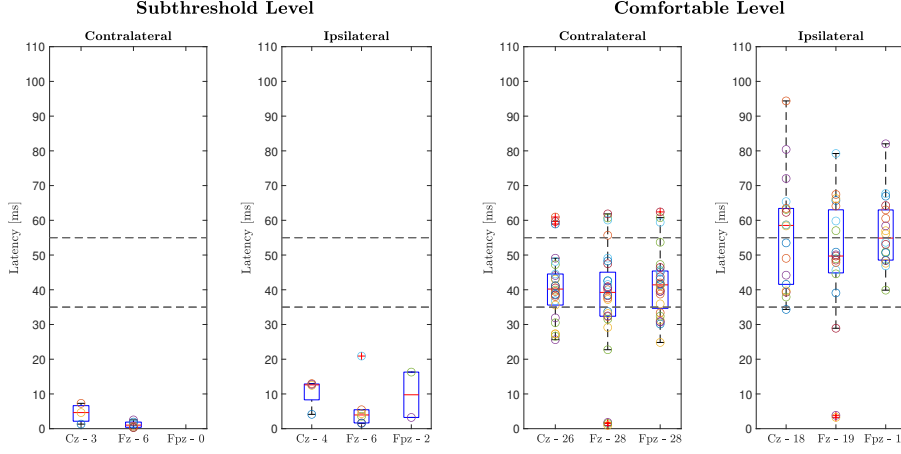


FIGURE 6.6: Latencies estimated by the pulse averaging method with averaging over a single pulse, individual processing

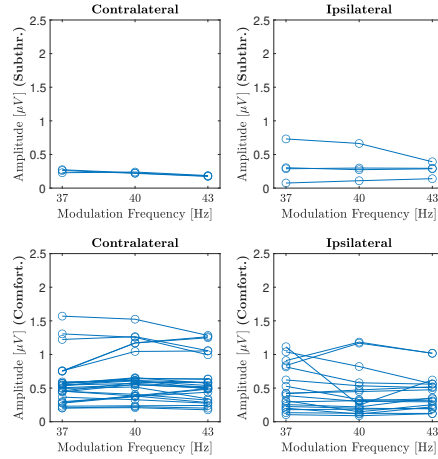


FIGURE 6.7: Amplitudes (reference: Cz) estimated by the pulse averaging method with averaging over a single pulse. Subthreshold (upper two subfigures) and comfortable stimulation level (bottom two subfigures)

6.4 Method 3: Nonlinear System Identification

This section displays the estimated latencies by the linear and nonlinear system identification (SI) approaches. In contrast to the previous section, its performance is compared to the linear SI approach, which is extensively compared to linear interpolation in [40].

6.4.1 Latency

Figure 6.8 shows the latencies as estimated by the linear SI (LSI) approach, which will serve as a baseline for the Volterra series-based, nonlinear SI (NLSI) approach. At subthreshold stimulation level, no false positive detections are observed for any reference electrode. At comfortable stimulation level, both contralateral and ipsilateral EEG channels display results for all recordings, except for the reference electrode Cz where 27 out of 30 and 17 out of 20 results are detected respectively. The median latency is located at the center of the expected range with limited estimations outside of the expected range. In contralateral EEG channels, a limited number of outliers are present, especially for reference electrode Fz and Fpz . In ipsilateral channels, a limited number of outliers above the upper bound of the expected range are observed.

Figure 6.9 shows the latencies estimated by the Volterra series-based SI approach. At subthreshold stimulation level, there are no false positive detections. At comfortable level, 27, 30, and 29 out of 30 results are detected in contralateral EEG channels. In ipsilateral EEG channels at this stimulation level, 16, 20, and 19 out of 20 results are observed. Again, the median latency is in the center at the expected range. The number of results at comfortable stimulation level is slightly decreased. The outliers at the bottom of the expected range from the SI approach are now inside. The outliers towards the upper bound are closer to the expected range.

At comfortable stimulation level, a Kruskal-Wallis test found a significance difference between the groups ($F(3, 83) = 15.52$ and $p = 0.0014$): LSI-contra, LSI-ipsi, NLSI-contra, NLSI-ipsi. Dunn's test found a significant different in the means between LSI-ipsi and LSI-contra ($p = 0.001$), NLSI-ipsi and NLSI-contra ($p = 0.003$), NLSI-contra and LSI-ipsi ($p = 0.001$) and NLSI-ipsi and LSI-contra ($p = 0.025$). No statistical difference between the means of NLSI-contra and LSI-contra ($p = 0.413$) and NLSI-ipsi and LSI-ipsi ($p = 0.85$) is observed.

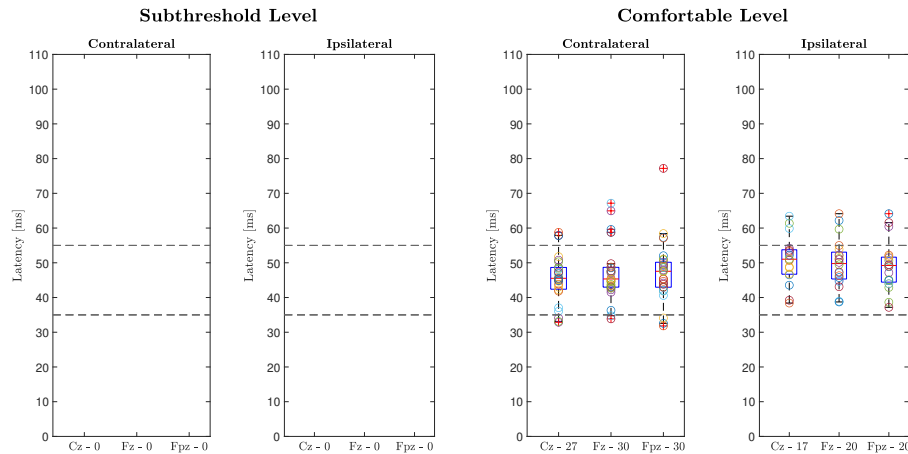


FIGURE 6.8: Latencies estimated by linear SI, joint processing, and masking of the stimulation pulses

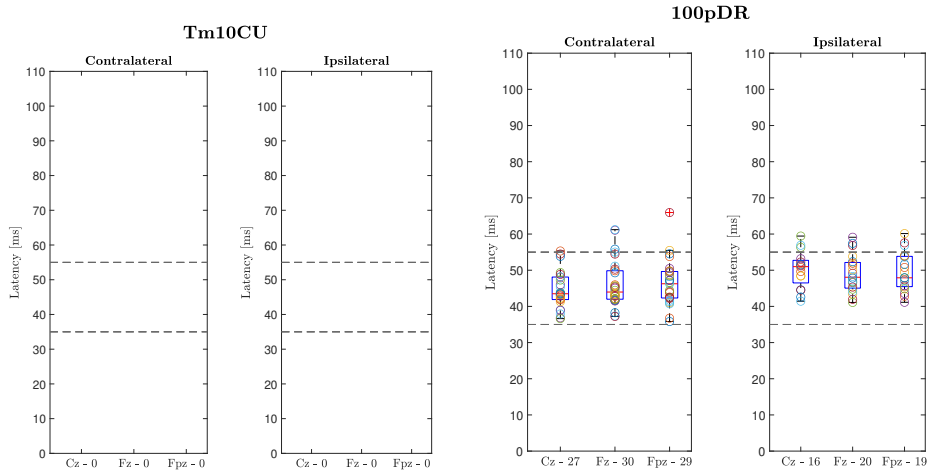


FIGURE 6.9: Latencies estimated by Volterra SI, joint processing, and masking of the stimulation pulses

6.4.2 Amplitude

Figure 6.10 shows the estimated amplitudes for reference electrode *Cz*. The results for the linear and nonlinear SI methods are displayed in Figure 6.10a and Figure 6.10b respectively. Both methods produce very similar estimated amplitudes, with slightly lower amplitudes being estimated for the nonlinear approach.

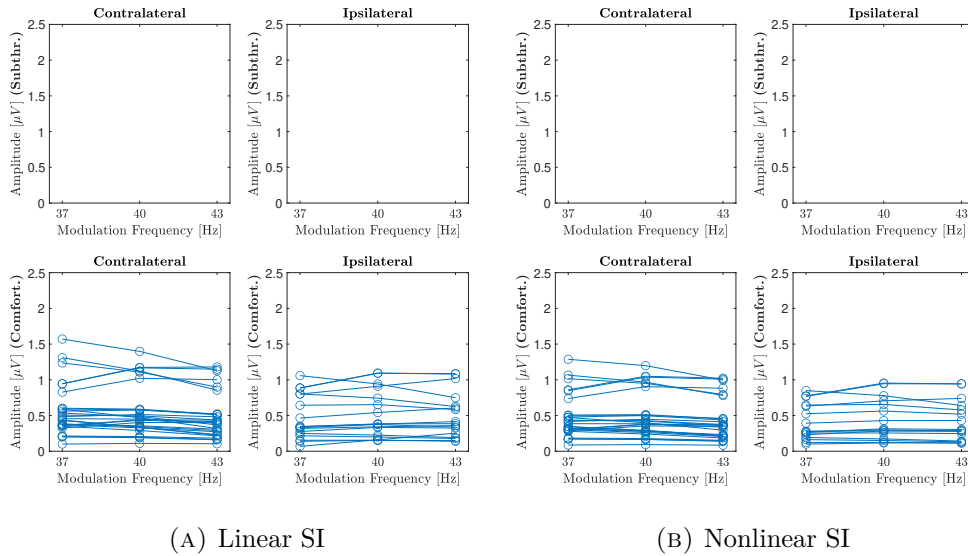


FIGURE 6.10: Amplitudes (for *Cz* as reference electrode) estimated by the linear and nonlinear SI approach. Subthreshold stimulation level (upper left and right) and comfortable stimulation level (bottom left and right) in each figure.

Chapter 7

Discussion

7.1 Introduction

This chapter discusses and interprets the results shown in [Chapter 6](#). This chapter studies the EASSR detection performance of each method by analyzing its estimated EASSR latencies, amplitudes, and false positive rate.

7.2 EASSR Detection Performance

This section discusses the EASSR detection performance of the methods developed within this thesis. This discussion is primarily based on the estimated latencies, of which the interpretation is further discussed in this section, as well as on the estimated amplitudes.

In [Chapter 2](#), the importance of latency as a discriminating property between artifact and EASSR is highlighted. The stimulation artifact propagates instantaneously, resulting in an artifact group delay or latency close to zero. In contrast, the generation of an EASSR requires processing time in the human brain resulting in a nonzero group delay or latency. This latency can be determined by analyzing the unwrapped phases of the estimated responses at different modulation frequencies. In case the estimated response shown in [Chapter 6](#) indeed reflects an EASSR, the latency should be in the range between 35 and 55 *ms*. [\[40, 38\]](#) Latencies close to zero reflect a dominant presence of the stimulation artifact. Latencies between zero and the lower bound of the expected range reflect improper separation. [\[40\]](#)

Note that excessively high latencies might reflect a dominant presence of the artifact as well. The phase of the stimulation artifact is stable at multiples of 180° , irrespective of the modulation frequency. [\[17\]](#) When the artifact phases at the different modulation frequencies are approximately equal, this results in a latency close to zero. However, when these artifact phases differ by 180° , latencies of about 80 and 120 ms are obtained based on the slope of the linear regression through the unwrapped phases $(180^\circ, 180^\circ, 0^\circ)$ and $(360^\circ, 180^\circ, 0^\circ)$ at the three modulation frequencies respectively.

7.2.1 Baseline: No Artifact Suppression

The latencies estimated by the response model without masking the stimulation pulses reflect the problematic nature of the stimulation artifact as stated in [Section 1.2](#). At subthreshold stimulation level, the false positive rate is considerably higher in ipsilateral (75 to 85 percent) as compared to contralateral EEG channels (13 to 30 percent). These results are expected since the artifact is known to be larger in ipsilateral as opposed to contralateral channels. [\[14\]](#) This result can also be interpreted in the context of the experimental artifact analysis in [Chapter 4](#), which observed an exponentially decaying amplitude of the artifact over distance.

At comfortable stimulation level, the results show that the stimulation artifact is sufficiently small in about half of the contralateral channels to detect a latency in the expected range without any form of artifact suppression. However, as the median latency is close to the lower bound of the expected latency range, the estimated response is most likely a mixture of EASSR and artifact in which the former dominates. In ipsilateral channels, the estimated latencies show a large spread. The excessively low ($< 10\text{ ms}$) and high ($> 75\text{ ms}$) latencies are indicative of artifact-dominated results. The intermediate latencies again are due to a mixture of EASSR and stimulation artifact.

The baseline performance also evaluated the effect of masking the stimulation pulses. The masking operation is beneficial in contralateral channels, both in terms of the false positive rate and the median latency. However, a number of estimated latencies are still artifact-dominated. The performance in ipsilateral channels on the contrary appears to have worsened and seems more artifact-dominated. When analyzing the spectra of the masked (containing the stimulation pulses) and non-masked (containing the interpulse intervals) segments of the mean epoch, it is observed that their components at the modulation frequency partially cancel out in some ipsilateral EEG recordings. It is hypothesized that the masking operation magnifies the asymmetry and hence the stimulation artifact in ipsilateral EEG recordings. In those recordings, the exponentially decaying tails are still dominantly present in the interpulse interval after masking the stimulation pulses. The increased amplitudes after masking in ipsilateral channels support this hypothesis.

7.2.2 Method 1: Time-Domain Artifact Suppression

The first method is the time-domain artifact suppression, which relies on the different temporal characteristics of the EASSR and stimulation artifact. The performance of this method must be evaluated in comparison to the results from the baseline without any form of artifact suppression and with masking of the stimulation pulses.

In contralateral channels, the time-domain artifact suppression method results in effective at both stimulation levels. At subthreshold levels, no false positive detections occur. At comfortable level, most estimated latencies are inside the expected range. The detection rate ranges from 73% to 87% depending on the reference electrode, and is increased for all reference electrodes except for *Cz*. The estimated EASSR

amplitudes are similar to the baseline performance. From these results, it can be concluded that in contralateral channels, the stimulation artifact predominantly consists of an exponentially decaying tail and a slowly varying bias in the interpulse interval.

In ipsilateral channels, the method halves the false positive rate compared to the baseline performance. The latencies remain low but are slightly elevated in comparison to the baseline performance. This indicates that although the estimated response is still a mixture of EASSR and stimulation artifact, the contribution of the former to this mixture is increased. The amplitudes are in a similar range. These results indicate the two templates - the exponentially decaying tail and the slowly varying bias - are on themselves insufficient to fully describe the stimulation artifact in ipsilateral channels. These results in ipsilateral channels demonstrate that more advanced artifact suppression methods are required, which tackle the fundamental causes of the stimulation artifact.

7.2.3 Method 2: Pulse Averaging

A second method is a novel approach and exploits the different effects of the pulse averaging operation on the stimulation artifact and EASSR. The performance of this method must be evaluated in comparison to the results from the baseline without any form of artifact suppression and without masking of the stimulation pulses.

At subthreshold stimulation level, this method strongly reduces the false positive rate, especially in ipsilateral channels. This confirms the preliminary results on the validation set presented [Table 5.1](#), which shows a reduction in artifact amplitude after pulse averaging.

At comfortable stimulation level, the detection rate varies between 85% and 95%. In contralateral channels, most estimated latencies are inside the expected range, although the data exhibit quite some variance. In ipsilateral channels, there is a clear increase in the median latency reflecting the EASSR characteristics. Most latencies are around or slightly above the upper bound of the expected range. The excessively high latencies are again most likely artifact-dominated. The amplitudes are elevated in contralateral channels and similar yet less stable in ipsilateral channels as compared to the amplitudes of the baseline and previous method.

The pulse averaging operation removes the inherent spectral component at the modulation frequency of the stimulation signal and attenuates any asymmetry. These obtained results are thus indicative that these two factors may indeed be the dominant causes of the stimulation artifact, thereby supporting the results obtained in the theoretical analysis of [Chapter 3](#). The increased variance of the estimated latencies and less stable amplitude estimation might be caused by the fact that this method is only able to attenuate any asymmetry, and does not remove it from the EEG recording. This method illustrates that a thorough understanding of the causes of and contributions to the stimulation artifact can be leveraged in artifact suppression methods. Although the method results in a rather low false positive rate and elevated

latencies at comfortable level, more advanced methods should be considered which are able to model the artifact more accurately and suppress it to a larger extent.

7.2.4 Method 3: Nonlinear System Identification

A third and last method extends the linear SI approach such that nonlinearities are included into the model. The performance of this nonlinear extension must be evaluated to the linear SI approach.

The existing linear SI approach results in an excellent performance, with no false positive detections at subthreshold stimulation level and most latencies inside the expected range at comfortable level. In contralateral channels, a number of latencies fall outside the expected range but are close to its bounds. This approach models the stimulation artifact as a FIR-filtered modulated Dirac pulse train, with a memory length exceeding the duration of the interpulse interval. Such a memory length is advantageous in the estimation of the artifact model. According to [16], the stimulation artifact exceeds the interpulse interval at a pulse rate of 900 pps. Note however that the two previous methods are not able to model a stimulation artifact which exceeds the interpulse interval. The fact that linear SI does model this property might thus contribute to its superior performance. Furthermore, since the input signal is a modulated Dirac train, the FIR coefficients can be loosely interpreted as a normalized artifact template. Indeed, these FIR-coefficients do exhibit an exponentially decaying character, which might explain the rather similar performance as compared to the time domain artifact suppression method in contralateral channels. However, the linear SI method does not restrict the template to an exponentially decaying tail and a bias term. This flexibility of the artifact model is assumed to be the primary cause for the increased detection rate and performance in ipsilateral channels.

The nonlinear Volterra-based SI shows similar performance to the linear SI method. At subthreshold stimulation level, the nonlinear approach preserves the lack of false positive detections. At comfortable stimulation level and in contralateral channels, almost all latencies now fall within the expected range. In ipsilateral channels, the outliers are also close to the upper bound of the expected range. The small performance increase due to the inclusion of nonlinearities in the artifact model is not fully unexpected. The theoretical analysis in [Chapter 3](#) revealed nonlinearities have a limited effect on the stimulation artifact at the modulation frequency in case a significant charge-imbalance is present. Furthermore, [Chapter 4](#) has shown that the stimulation artifact at the modulation frequency scales approximately linearly with the stimulation level. Nevertheless, the same experimental analysis did show the presence of nonlinearities in the EEG recordings. The amplitudes estimated by the Volterra SI approach are slightly lower but appear more stable in comparison to the linear approach. Since no ground truth is available, it is unclear whether these lower but more stable amplitude values reflect a more accurate modeling.

Chapter 8

Conclusion and Future Work

8.1 Conclusion

This thesis dissertation has studied methods to detect EASSRs in EEG recordings which are contaminated by stimulation artifacts originating from cochlear implants. The stimulation artifact has been characterized both theoretically and experimentally. The results of this characterization are then used to guide the development of EASSR detection algorithms, of which the performance is evaluated on EEG recordings acquired from CI recipients at two different stimulation levels. This final chapter summarizes the main findings of the thesis in order to answer the two research questions presented in [Chapter 1](#).

8.1.1 Artifact Characterization

The first research question read: "Which nonidealities and nonlinearities cause and/or contribute to the stimulation artifact, and what are their defining characteristics?"

The theoretical analysis in [Chapter 3](#) has shown that the ideal stimulation signal does not contain a component at the modulation frequency. In literature [[16](#), [40](#), [27](#), [3](#)], this statement is often obtained through simulations and the main motivation as to why nonidealities and nonlinearities are required to explain the presence of the stimulation artifact. In this thesis, the practical stimulation signal is proposed as a more accurate signal representation, as it incorporates the charge-balance constraint which must be satisfied in practice [[51](#)]. It is shown that this practical stimulation signal inherently contains a stimulation artifact at the modulation frequency. This implies nonidealities and nonlinearities are, strictly speaking, no longer required to explain the presence of the artifact. However, in case these effects do occur, the stimulation artifact at the modulation frequency is amplified. The theoretical analysis shows that any form of charge-imbalance or pulse asymmetry amplifies the inherent stimulation artifact. In terms of nonlinearities, only second order nonlinearities are able to result in a considerable contribution to the stimulation artifact when a limited amount of charge-imbalance is observed.

Chapter 4 has validated that the practical stimulation signal is a more accurate signal representation. It shows that the pulse profiles are indeed flat and that the stimulation artifact increases in magnitude with the modulation frequency. Similar to [16], a pulse asymmetry has been observed. In this thesis, the nature of this pulse asymmetry is further studied. The results show that, next to a constant offset, the observed pulse asymmetry scales predominantly linearly with the pulse amplitude, although second order and third order nonlinearities are observed in the scaling behavior of the pulses as well. A connection between pulse asymmetry and the stimulation artifact could not be analyzed due to the decaying nature of the signal. Similar to [22, 27], nonlinearities have been observed in the mean epoch of the EEG signal at maximal stimulation level. In this thesis, the first, second and third order components are quantified and presented in an overview. The analysis indicates a consistent presence of second order nonlinearities in the mean EEG epoch. However, as the artifactual component at the modulation frequency is observed to scale predominantly linearly with the stimulation level, their effect in the context of EASSR detection is assumed to be limited.

8.1.2 Artifact Suppression Methods

The second research question read: "How can the knowledge of these nonidealities and nonlinearities be leveraged in the development of and extensions to methods which aim to separate the stimulation artifact and EASSR?".

To this end, three methods have been developed, each focusing on a different aspect of the artifact. A first method aims to exploit the difference in temporal characteristics of the artifact and EASSR. It can be interpreted as an alternative implementation of Kalman filter-based approaches [14, 34]. This method is effective in contralateral channels, while ipsilateral channels are still artifact-dominated at comfortable level. The false positive rate in ipsilateral channels did halve however. These results indicate that the exponentially decaying tail and slowly varying bias-term are important components of the artifact, but are on themselves insufficient to adequately model the artifact. Methods which tackle the fundamental causes and/or contributions to the artifact are required.

A second method is a novel approach and exploits the different effects of averaging each pulse on the EASSR and stimulation artifact to suppress the latter. The pulse averaging operation removes the inherent component of the stimulation artifact at the modulation frequency and attenuates any form of charge-imbalance or nonlinearity. This method is effective in contralateral channels. In ipsilateral channels the median latency is elevated while the estimated latencies do however exhibit a large spread, indicative of imperfect separation. This spread is most likely caused by the fact the asymmetry is attenuated and not removed from the EEG recording. Since the removal of the inherent component and the attenuation of the pulse asymmetry result in this performance, it shows their causation of and/or contribution to the stimulation artifact, as expected based on the theoretical artifact analysis.

The third and final method incorporates nonlinearities in the artifact model of the

linear SI method introduced in [40]. The linear approach already incorporated the pulse asymmetry by selecting a Dirac train as the input signal to the artifact model. This thesis includes nonlinearities in the model as well. In contrast to the two previous methods, the artifact models in these methods take into account that the artifact has not fully decayed at the end of the interpulse interval. Furthermore, they can be interpreted as a more flexible variant of the time domain artifact suppression method. The linear SI approach results in excellent performance in all channels at both stimulation levels, although a number of latencies are outside the expected range. The nonlinear SI extension enhances this method and increases the number of estimated latencies inside the expected range. The performance increase is however subtle and difficult to evaluate as no ground truth EASSR characteristics are present. This result is however not fully unexpected. Although the experimental artifact analysis indicates the presence of second order nonlinearities, it shows that the stimulation artifact scales linearly with the stimulation level. Especially the comparison of the linear and nonlinear SI is troubled by the absence of ground truth EASSR characteristics.

The last two methods show that leveraging theoretical knowledge of the artifact and incorporating nonidealities and nonlinearities into artifact suppression methods does result in an improvement as compared to the baseline performance or relying on known temporal artifact characteristics.

8.2 Future Work

This final section provides suggestions for future work, both in the context of artifact characterization and artifact suppression methods.

8.2.1 Artifact Characterization

The experimental analysis presented in [Chapter 4](#) uses a head phantom consisting of a 0.2 % saline solution to mimic the artifact propagation through the human head. Despite the fact that [29] has shown that it is a suited medium for this application [29], it remains a rather coarse approximation of reality. Future work in the context of artifact characterization can extend this head phantom by including layers representing the skull and scalp and investigating their effects. Other possibilities to obtain a more accurate artifact characterization include measurements on a cadaver head, as carried out in [22], or through simulations using advanced head models.

The stimulation signal used in the experimental characterization contains only two modulation frequencies, ensuring a sufficient distance is preserved between first and high order spectral components in the frequency domain. However, modulating the stimulation pulse train with multiple modulation frequencies allows to identify the scaling behavior of the first order artifact components with modulation frequency more accurately. Future work can apply the experimental artifact characterization analyses presented in this thesis to such stimuli.

8.2.2 Artifact Suppression Methods

The second method presented in this thesis averages each pulse to remove the inherent component of the stimulation artifact. However, any form of asymmetry is not removed but only attenuated through pulse averaging. Future work can study whether knowledge about this asymmetry, through features such as the pulse asymmetry measure as introduced in [Chapter 4](#), can be leveraged to fully remove the now only attenuated asymmetry component.

Lastly, the nonlinear SI approach has shown only subtle improvements in performance as compared to the linear SI approach. Future work can study whether the performance differences are more pronounced at lower stimulation levels, or for EEG recordings that are not acquired using a hyper-rate system.

An important drawback of the SI approaches is their reliance on three EEG recordings, in contrast to the first and second methods. It is hypothesized that the artifact model predominantly relies on the scaling of the stimulation artifact with the modulation frequency. Future research can focus on adequately combining multiple modulating frequencies in a single stimulation signal, such that the estimation of the artifact model can be performed based on a single EEG recording.

Appendices

Appendix A

Effect of Polynomial NonLinearities

This appendix contains the mathematical derivations of the effect of static polynomial nonlinearities on the input spectrum.

The degree of the polynomial term is referred to by the letter s , instead of the more commonly used n to avoid ambiguity with the index of the characteristics of the negative pulse.

For both the ideal and practical stimulation signal, the effect of polynomial nonlinearities is studied by observing their effects on the positive and negative pulses separately. Such an approach shows that the same derivation can be used as for the stimulation signals in [Chapter 3](#) when the positive and negative pulse amplitudes A_p and A_n respectively are raised to the power s , and the modulation signal $m(t)$ is replaced by $m(t)^s$. The next two subsections explore the effect of nonlinearities on the biphasic, cathodic-first pulse $p(t)$, and the effect on the modulating signal $m(t)$.

A.0.1 Effect on the Biphasic, Cathodic-First Pulse

Due to the pulsed nature of this biphasic, cathodic-first pulse $p(t)$, the effects of polynomial nonlinearities only concern the pulse amplitudes:

- for odd s : $p(t)$ undergoes a simple scaling operation. That is, the negative and positive pulse will have amplitudes A_n^s and A_p^s respectively. The spectrum of the biphasic, cathodic-first pulse derived earlier remains valid when this amplitude scaling is taken into account.
- for even s : the positive pulse amplitude A_p is raised to the power s . As the negative pulse amplitude A_n is raised to the power s , they will become positive. The spectrum of the biphasic, cathodic-first pulse derived earlier remains valid due to the sign-inclusion in the parametrization of the negative pulse amplitude. Note that polynomial nonlinearities of even order result in a DC-component and thus charge-imbalance.

In both cases, it can be concluded that the spectrum of the pulse waveform $p(t)$ is given by:

$$P_s(f) = A_p^s \cdot T_p \cdot \frac{\sin(\pi \cdot f \cdot T_p)}{\pi \cdot f \cdot T_p} \cdot e^{-j \cdot \pi \cdot f \cdot (T_p + T_i)} + A_n^s \cdot T_n \cdot \frac{\sin(\pi \cdot f \cdot T_n)}{\pi \cdot f \cdot T_n} \cdot e^{j \cdot \pi \cdot f \cdot (T_n + T_i)} \quad (\text{A.1})$$

A.0.2 Effect on Modulating Signal

This subsection analyzes the effect on the modulating signal $m(t) = A_m \cdot (1 + D \cdot \cos(2\pi f_m t + \phi_m))$ when it passes through a static polynomial non-linearity. To ease notation, the argument of the cosine will be replaced by x , that is $x = 2\pi f_m t + \phi_m$, such that $m(t) = A_m(1 + D \cdot \cos(x))$. The objective of the analysis is to determine the spectral component of $m(t)^s$ at the modulation frequency f_m .

In general, the power of a sum of two signals y and z can be expressed as:

$$(y + z)^s = \sum_{k=0}^s \binom{s}{k} y^{s-k} z^k = \frac{s!}{k!(s-k)!} y^{s-k} z^k \quad (\text{A.2})$$

Using this expression, the s -th power of $m(t)$ can be expanded:

$$m(t)^s = A_m^s (1 + D \cdot \cos(x))^s = A_m^s \sum_{k=0}^s \binom{s}{k} \cdot D^k \cdot \cos(x)^k \quad (\text{A.3})$$

Our main interest lies in the frequencies of $m(t)^s$, i.e. an expansion in terms of $\cos(kx)$ instead of $\cos(x)^k$. Therefore, $\cos(x)^k$ is expressed in terms of $\cos(kx)$. For this purpose, Equation A.2 can be applied after expressing a cosine as the sum of two complex exponentials:

$$\cos^k(x) = \frac{1}{2^k} (e^{jx} + e^{-jx})^k \quad (\text{A.4})$$

Expanding this expression allows to rewrite the power of a cosine as a sum of cosines oscillating at multiples of the original modulation frequency [1]:

$$\cos(x)^k = \frac{1}{2^k} \sum_{k'=0}^k \binom{k}{k'} \cos((k - 2k') \cdot x) \quad (\text{A.5})$$

This expression can be used to rewrite Equation A.3:

$$m(t)^s = A_m^s \sum_{k=0}^s \binom{s}{k} \cdot D^k \cdot \frac{1}{2^k} \sum_{k'=0}^k \binom{k}{k'} \cos((k - 2k') \cdot x) = A_m^s \sum_{s=0}^k b_k \cos(k \cdot x) \quad (\text{A.6})$$

When considering the modulating signal $m(t)$ raised to the power s , the resulting signal consists of a sum of cosines each raised to a power ranging from 0 to s , thereby introducing components at the DC, the fundamental modulation frequency and all harmonics up to s -th order. The analytical expression for the coefficient of each frequency component is abstracted in the symbol b_k . Simulations in MATLAB show that the expression provided in Equation A.6 is valid.

A.0.3 Overall Effect

Similar to Equation 3.19, the expression for $G_{pract,s}(nf_m)$ is given by:

$$G_{pract,s}(nf_m) = P_s(f_m) f_c \frac{A_m^s b_n}{2} e^{jn\phi_m} \quad (\text{A.7})$$

in which b_n expresses the coefficient corresponding to the n th harmonic of the modulation frequency. For the ideal stimulation signals, a similar relationship as Equation 3.11 is obtained where A_p and A_n are raised to the power s , and where the effect of b_n is included. Figures resulting from these expressions are presented in the text.

Appendix B

Supplementary Results

Figure B.1 shows the estimated latencies by the response model without any form of artifact suppression, in case the three EEG recordings at a single stimulation level are processed jointly.

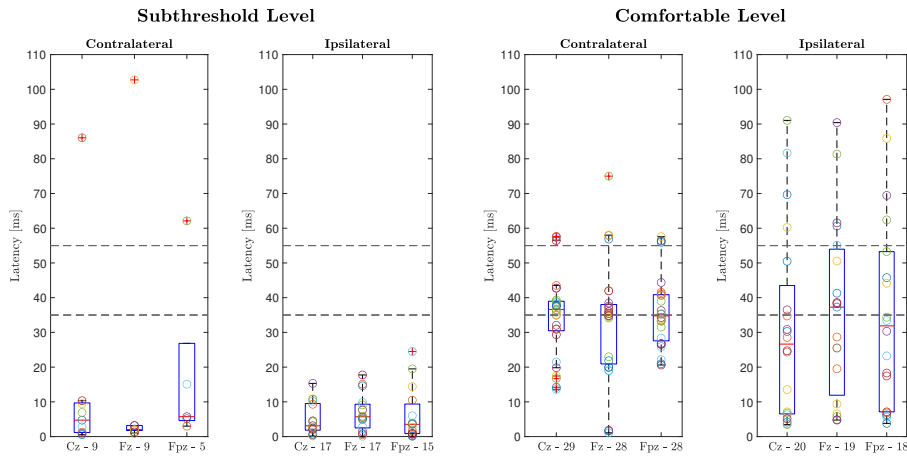


FIGURE B.1: Latencies estimated by the response model without artifact suppression, joint processing

Figure B.2 shows the estimated latencies by the response model without any form of artifact suppression when the stimulation pulses are masked, in case the three EEG recordings at a single stimulation level are processed jointly.

Figure B.3 shows the estimated amplitudes by the response model without any form of artifact suppression without (left) and with (right) masking of the stimulation pulses, in case the three EEG recordings at a single stimulation level are processed jointly.

B. SUPPLEMENTARY RESULTS

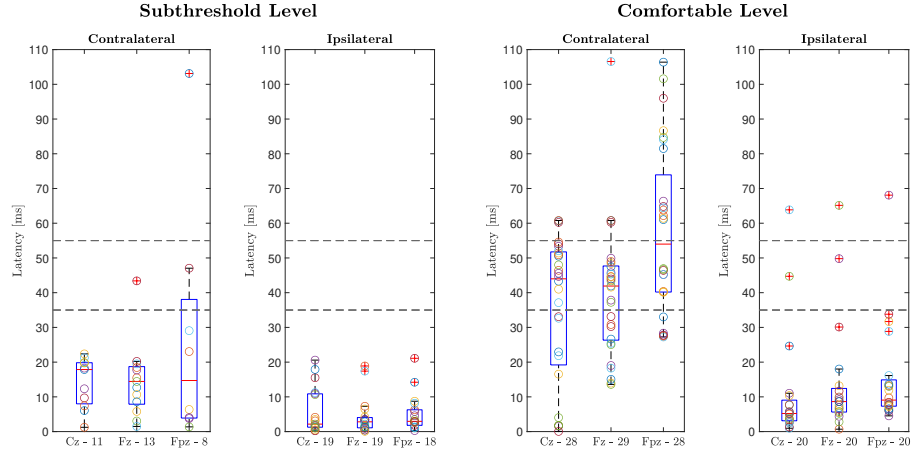


FIGURE B.2: Latencies estimated by the response model without artifact suppression, joint processing, and masking the stimulation pulses

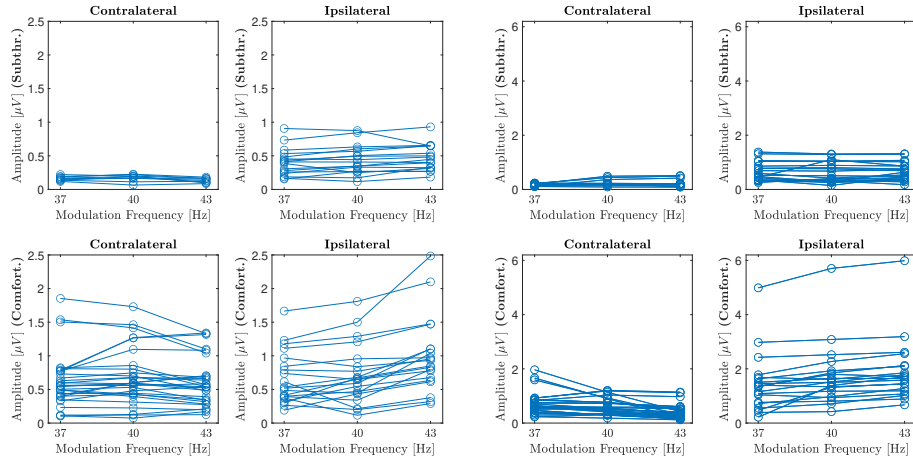


FIGURE B.3: Amplitudes estimated by the response model without artifact suppression, joint processing without (left) and with (right) masking the stimulation pulses

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