A closer look at stimulation thresholds and spread of excitation in cochlear implants: recording aspects and clinical implications

Biesheuvel, J.D.

CHAPTER

1

General introduction

Hearing is an important element in communication, social interaction, and human wellbeing. It is, therefore, essential to identify hearing loss in an early stage and to rehabilitate hearing loss adequately. Hearing loss can generally be rehabilitated with a hearing aid, except if there is a severe sensorineural hearing loss. Sensorineural hearing loss is often associated with damaged or deficient cochlear hair cells, resulting in an inability to translate sounds into neural signals traveling toward the brain. In that case, just sound amplification by a hearing aid is no longer effective and other means of rehabilitations need to be sought. Some decades ago, the population of deaf and hard of hearing people was dependent on written language, sign language or lip reading. However, with the advent of cochlear implants (CIs) new perspectives arose (Shannon 1983). A CI is a device that delivers sound directly to the auditory nerve by electrical stimulation via an electrode array in the cochlea. Although CIs do not work equally well for everyone, most people with a CI can again communicate via spoken language.

1.1. Cochlear implant

A CI consists of two parts: (1) an external part, which is called the sound processor and is worn on the ear, and (2) an internal part, which is the actual implant located under the skin. Figure 1.1 shows the different components of a CI and their position relative to the human anatomy. The first step in hearing with a CI is the recording of sound signals by the microphones of the sound processor. Next, the sound is pre-processed, e.g., noise is reduced and speech is amplified. The optimized sound signal is then divided over different frequency bands using bandpass filters. The sound energy per frequency band, typically coded by the envelope of the signal, forms the basis for calculating the stimulation pattern across the spectral channels. After calculating the stimulation pattern, the pattern is sent wirelessly to the implant via a coil located in the headpiece. In the implant, the stimulation pattern is transformed into electrical current pulses. These pulses go through multiple wires bundled in the electrode lead to different electrode contacts in the cochlea, where they deliver frequency specific stimulation. Finally, the electrical pulses will stimulate the auditory nerve and the CI-user perceives a sound. The CI uses the tonotopical organization of the cochlea, whereby high-frequency sounds are encoded at the base of the cochlea and low-frequency sounds in the apex of the cochlea.

1.2. Electrically evoked compound action potential

After electrical stimulation, the current spreads through the cochlea and excites multiple nerve fibers. In each excited nerve fiber, an action potential arises, which is a wave of electrical charge traveling over the nerve fiber membrane towards the brain. Due to the short and strong stimulus, all action potentials are generated simultaneously and together they form

an electrically evoked compound action potential (eCAP). The eCAP is a measurable electrical potential that represents the synchronous firing of multiple nerve fibers (Abbas et al. 1999; Hughes 2013). It is important to realize that the eCAP is a complex result of several factors: the number of firing nerve fibers, the position of the measuring electrodes, synchronicity of the excitation and the electrical conduction of the tissue (Mens 2007).

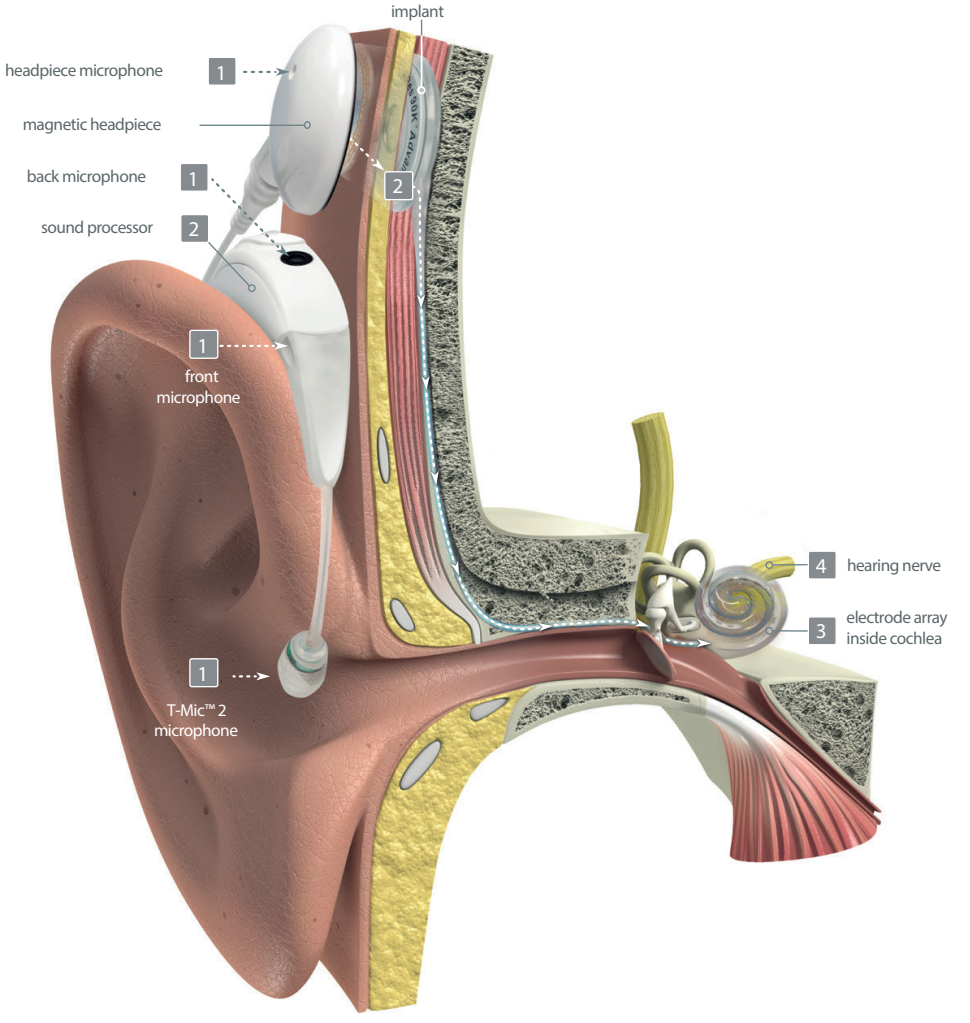

Figure 1.1. A cochlear implant consists of several components: microphones (1), sound processor and implant (2), and the electrode array in the cochlea (3). Via these components acoustic sounds are converted into electrical signals that directly stimulates the auditory nerve (4). Image courtesy of Advanced Bionics.

1.2.1. Recording eCAPs

All modern CIs have a built-in telemetry function for recording eCAP signals (Hughes 2013). Figure 1.2 schematically shows how an eCAP signal can be measured. A CI contains a current source that provides electrical stimulation via one of the electrode contacts located in the cochlea. Subsequently, an eCAP arises, which can be measured via an adjacent electrode contact and a reference contact located outside the cochlea. In general, the eCAP is measured using an intra-cochlear contact close to the source, i.e., the excited neurons. This is favorable for the amplitude of the signal and therefore for the signal-to-noise ratio. The recorded signal can be read-out via the speech processor and a computer. Typically, the eCAP is recorded as a waveform with a negative peak (N1) followed by a positive peak or plateau (P1). The amplitude of the eCAP is measured from N1 to P1 and can reach values up to 1.5 mV.

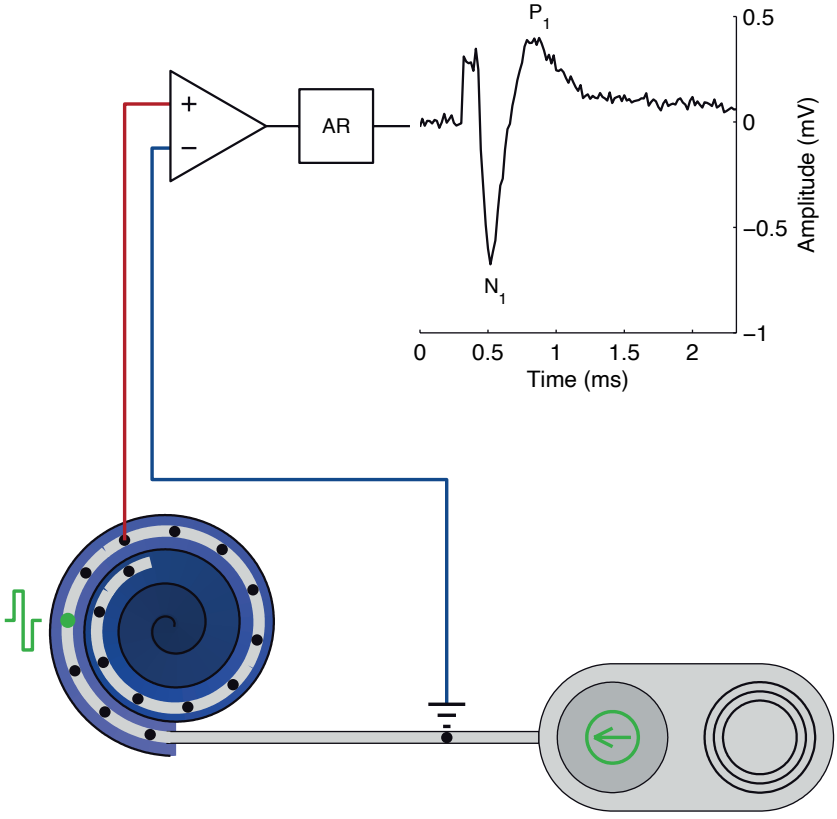

Figure 1.2. Schematic representation of an eCAP measurement. The CI (gray) has a current source (green arrow) that provides electrical stimulation (green pulse) via one of the electrode contacts in the cochlea (blue). Due to electrical stimulation, there arises an eCAP (black signal in the graph) which can be measured using the telemetry function of the CI, including a neural amplifier (represented by the triangle) and an artifact rejection method. CI indicates cochlear implant; eCAP, electrically evoked compound action potential, AR, artifact rejection.

Two different electrical signals play a role in recording eCAPs: the stimulus and the eCAP signal. The stimulus is typically a biphasic pulse with an amplitude of a few hundred microamperes. A biphasic pulse is charge-balanced, which means that the delivered net charge is zero in order to prevent tissue damage due to charge build-up. The stimulus creates a large electrical potential (factor 10,000 greater than the eCAP) which has a disruptive effect on the measurement amplifier and causes an artifact in the eCAP recording. An amplifier is necessary to increase the relatively small eCAP signal in order to make optimal use of the dynamic range of the analog-to-digital converter. However, the stimulus potential exceeds the input range of the amplifier, consequently causing saturation of the amplifier and blocking the signal from passing through. This blocking is temporary and lasts generally a bit longer than the stimulus duration (50-100 μs). After the stimulus artifact has ended, the magnitude of the potential will decrease exponentially and as soon as it is smaller than the input range of the amplifier the amplifier will provide a reliable output again.

1.2.2. Artifact rejection paradigm

The stimulus artifact thus has a disruptive effect on the eCAP recording. To minimize this effect, the recording contact is often chosen at some distance from the stimulating contact. However, a larger distance between the recording contact and the firing nerve fibers negatively affects the amplitude and the shape of the eCAP. In practice, a distance of one or two physical contacts between the stimulating and recording contacts is often chosen as optimum. Another difficulty is that the eCAP already occurs while the amplifier is still in the recovery phase (Figure 1.3). So, the eCAP is (partly) hidden in the stimulus artifact and these two signals must be separated in order to enable a proper eCAP assessment. Over years, several methods have been developed to separate the eCAP signal from the stimulus artifact (Miller et al. 2000; Klop et al. 2004; Hughes et al. 2016; Baudhuin et al. 2016), whereby forward masking (FM) and alternating polarity (AP) were most commonly used.

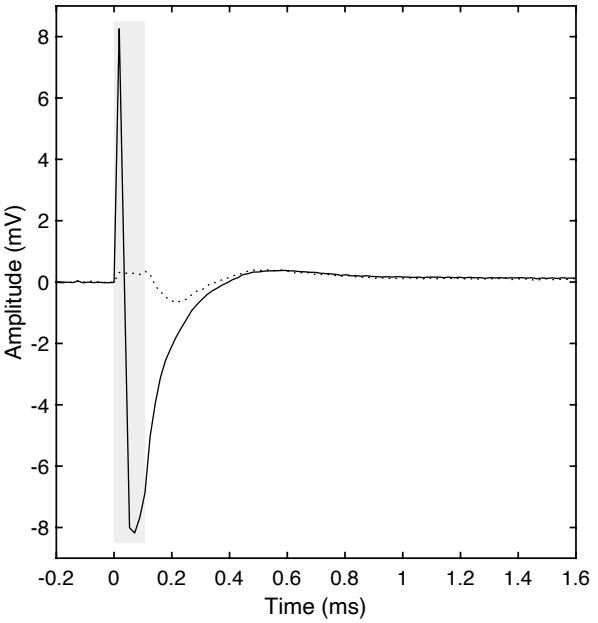

Figure 1.3. As long as the stimulus lasts (gray area) the neural amplifier delivers an unreliable output. The output signal (black line) looks like the stimulus potential, but valuable information about the eCAP is totally blanked. When the stimulus has ended, the stimulus potential decreases exponentially and meanwhile the eCAP (dotted line) occurs. This eCAP can be extracted from the recorded signal using an artifact rejection method. eCAP indicates electrically evoked compound action potential.

The FM paradigm makes use of the refractory properties of the auditory nerve to separate the eCAP from the stimulus artifact. The method used two different stimuli: a masker stimulus and a probe stimulus. Using a combination of these stimuli, four different recordings can be made, which can be subtracted from each other to extract the eCAP (Figure 1.4). First, the masker stimulus (M) is delivered, which results in a stimulus artifact of the masker including an eCAP signal. Then the masker and the probe (MP) are delivered with a masker-probe interval time of typically 300-500 µs. Due to the masker, the nerve fibers are in their absolute refractory state and are insensitive to the probe stimulus. This results in a recording that contains twice a stimulus artifact and one eCAP (after the masker only). When all nerve fibers are recovered from their refractory state, the probe (P) is delivered again resulting in a probe stimulus artifact including an eCAP. The eCAP can now be eliminated from these three recordings by calculating: eCAP = M + P - MP. Finally, a fourth measurement is often subtracted from the measurement signals, the so-called 'system signature'. In this recording, the stimulus levels are set to zero which leads to a recording that contains system properties such as interference and noise, for which can be corrected (Frijns et al. 2002).

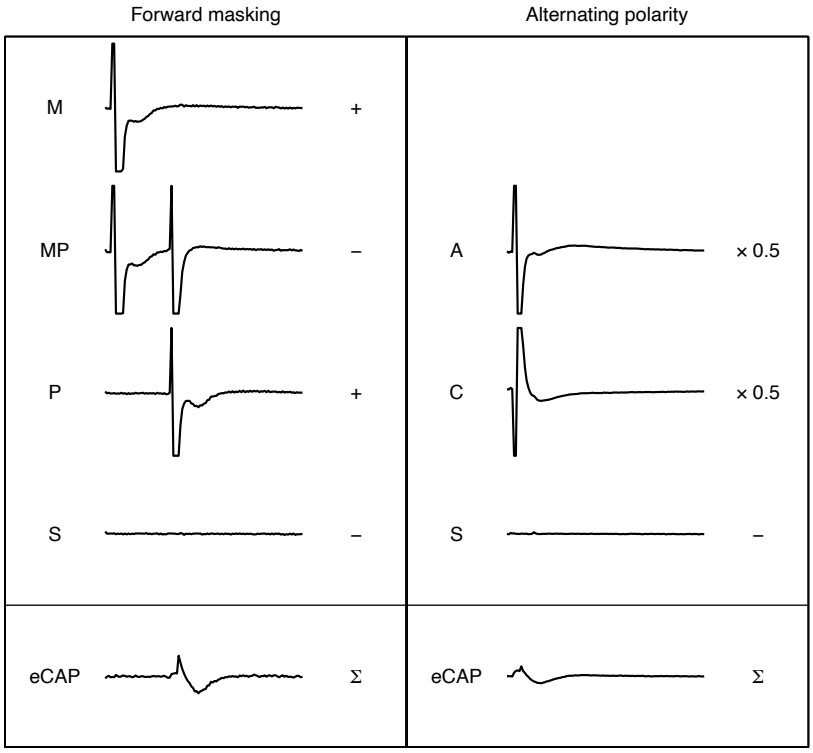

Figure 1.4. Graphical representation of two commonly used artifact rejection paradigms: forward masking (left column) and alternating polarity (right column). The forward masking paradigm consists of four different frames (M, MP, P and S) which can be combined mathematically to extract the eCAP from the stimulus artifact. The AP paradigm consists of three frames (A, C and S) which also can be combined to extract the eCAP. eCAP indicates electrically evoked compound action potential.

The AP paradigm makes use of the eCAP property that the polarity of the eCAP signal does not change when the stimulus polarity is reversed, while the stimulus artifact adopts the polarity of the stimulus. This property can be used to filter the eCAP from the measurement signal (Figure 1.4). For that purpose, two recordings were obtained. First a recording using a biphasic stimulus with a positive phase followed by a negative one (anodic-first, A), and second a recording using a negative phase followed by a positive one (cathodic-first, C). Both stimuli result in an eCAP with the same polarity, while the polarity of the stimulus artifact is opposite. Now the eCAP can be recovered by calculating: eCAP = (A + C) / 2. Lastly, the recording can be corrected for the system signature (S).

1.3. ReaSONS project

Although a rejection paradigm reveals a major part of the eCAP signal, we still do not know what the real shape of the eCAP is in the timespan that the amplifier is saturated and delivers an unreliable output. Considering all difficulties in recording eCAPs, we can conclude that

there is need for a method that enables measuring eCAPs without being bothered by the stimulus artifact. The Real-time Sensing Of Neural Signals project pursues this. The ReaSONS project is funded by the Technological Sciences Foundation under number 11693. The project consists of two parts: (1) developing a new neural amplifier for reliable and accurate eCAP measurements and (2) investigating the clinical applicability and relevance of eCAP measurements. These two components have been elaborated by respectively a PhD student at Technical University Delft and a PhD student at the Leiden University Medical Center. A brief description of the development of the neural amplifier is given below, while the research focusing on the human eCAP measurements will be the content of this thesis.

The new neural amplifier developed at the Technical University Delft uses a compression technique to prevent amplifier saturation. As soon as the recorded signal grows beyond the input dynamic range of the amplifier, the input signal will be corrected (shifted downward) so that it does not exceed the dynamic range of the amplifier. This technique is also called companding. By precise registration of all corrections, the original signal can be reconstructed later, after conversion of the signal to the digital domain by an analog to digital converter. Doing this, the new amplifier has a dynamic range of 126 dB, so that both the stimulus artifact (up to 20V) and the neural response (up to 10μV) can be registered reliably (Bes et al. 2010). After signal reconstruction and artifact rejection, there remains an eCAP signal that has been measured reliably throughout the whole recording time. In addition, the new amplifier is relatively small compared to the electronic components in current CIs. This means that in the future multiple amplifiers will fit into the CI housing, and eCAPs can be measured simultaneously on several electrode contacts. So, the application of the new measuring amplifier seems promising for future research in the field of eCAPs.

1.4. Content of this thesis

This thesis focuses on the clinical applicability and the relevance of eCAP measurements. The goal is to gain more insight into CI functioning and into the effect of electrical stimulation on the auditory nerve. More knowledge about these topics may be useful to further improve CI technology, potentially leading to better CI listening experience.

The first study of this thesis is about the applicability of eCAPs as an objective measure to guide CI fittings. For some CI users, e.g., small children, it can be difficult to find the best CI fitting, because they do not provide adequate feedback to adjustments made by the audiologist. Therefore, it would be valuable if there is an objective tool that helps the audiologist to guide these fittings. With the improvement of the CI telemetry functions, it has been suggested that eCAP measurements may ease this fitting challenge (Brown et

al. 2000). In the last decades, several studies concluded that the eCAP threshold, which is the minimum amount of current required to generate an eCAP, would be a good predictor of the T-level at the same electrode contact (Botros & Psarros 2010; Kaplan-Neeman et al. 2004; Lai et al. 2009; Mittal & Panwar 2009; Morita et al. 2003; Muhaimeed et al. 2010; Pedley et al. 2007; Walkowiak et al. 2011) while others were less conclusive (Franck 2002; Smoorenburg et al. 2002; Potts et al. 2007; Holstad et al. 2009; Jeon et al. 2010; Raghunandhan et al. 2014). Inspired by the contradictory outcomes in the literature, we perform a systematic literature review to clearly state how much evidence there is that eCAPs can be used in fitting CIs **(Chapter 2)**. Another question we have regarding eCAP thresholds is: Why is there often no relationship between the eCAP thresholds and the subjective hearing thresholds of the CI user, while most researchers and clinicians expect this relationship? We may be missing important details of the eCAP because these details are not registered by the current measurement systems. On the other hand, it is also possible that the outcome measures (eCAP thresholds and subjective thresholds) are not precise and accurate enough, as there is a lack of reporting measurement errors in the literature. To further investigate this, we looked at the precision of the eCAP thresholds **(Chapter 3)**.

Besides eCAP thresholds, it is also possible to derive the spread of neural excitation (SOE) from eCAP recordings. SOE is a measure linked to the specificity of the electric-neural interface, and can be estimated objectively from spatial forward masking (SFM) curves (Cohen et al. 2003; Abbas et al. 1999; Hughes & Abbas 2006b; van der Beek et al. 2012). With knowledge about SOE, stimulation strategies can be improved, e.g., by making them more selective and having more control about the induced pitch. The expectation is that selective stimulation is better for the audibility of different sounds and therefore for speech understanding. However, to date, no clear relationships between eCAP-based SOE and speech performance outcomes have been found. In the context of this thesis, we will critically look at the measure of SOE used thus far, that is, the width of the SFM curve. We think that the width of the SFM curve is not an adequate measure of SOE, and we propose a new method to objectively determine the excitation patterns and SOE of individual electrode contacts in CI **(Chapter 4)**. Using that method, we can also study the effect of stimulus level on excitation patterns in more detail **(Chapter 5)**.

The final study of this thesis focuses on a new method for testing pitch discrimination in CI users. Several studies have investigated whether there is a relationship between the eCAP and psychophysical measures such as spatial resolution (Firszt et al. 2007; Koch et al. 2007; Snel-Bongers et al. 2012). In these studies, the pitch discrimination of CI users was often

measured very accurately, but due to time limitations it was collected on a limited number of electrode contacts only. We would like to have a method that tests pitch discrimination on all electrode contacts in a relatively short test time. This knowledge can be used to further improve stimulation strategies and it can be used in studying SOE across the whole electrode array. We develop a new method for testing channel discrimination across all contacts of the electrode array, and we evaluate how well the channel discrimination ability from CI recipients correlate with their speech perception **(Chapter 6)**.

Finally, the thesis ends with a general discussion, wherein we discuss some complexities in recording eCAPs and elaborate on the future perspectives of the eCAP measures **(Chapter 7)**.