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Chapter 1

Introduction and outline of the thesis

The Dutch population counts about 12,000 adults and children with severe to profound hearing loss (2012). Hearing aids are a poor solution for this group. A paramount opportunity of rehabilitation is a cochlear implant. Cochlear implant users regain part of their hearing by direct electrical stimulation of the auditory nerve. Experiments with electrical stimulation of the auditory system started several centuries ago with the electrical stimulation by a battery (Volta 1800). Technological improvements and the increasing computing capabilities of computer chips have led to new possibilities and improvements of speech coding strategies. Nowadays, manufacturers develop multi-channel cochlear implants with advanced speech coding strategies.

All current multi-channel cochlear implant systems have the same basic components and functions as the "Chorimac", developed in the mid-Seventies by Bertin for Chouard. A cochlear implant consists of an external and internal part. The

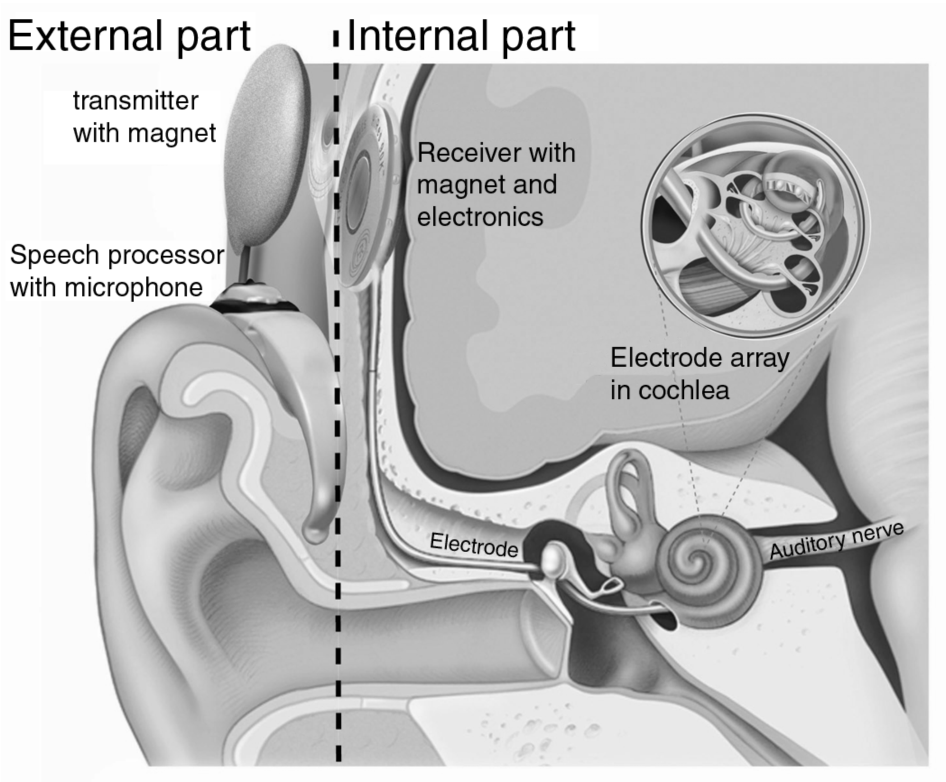

Figure 1. *Graphical representation of the basic components of a cochlear implant system with the internal and external part.*

external part consists of an externally worn speech processor and a microphone (Figure 1). The microphone captures incoming sounds, and the sound signal is processed in a speech processor. The speech processors can be divided into two groups, the body worn and the behind the ear processor. The processors filter the auditory signal into separate frequency bands, corresponding to each active channel of a cochlear implant. With a specific speech coding strategy a digital code is generated. This coded auditory signal is sent from the speech processor via a head piece containing a transmitting coil to the internal part. The transmitter is held in place by a small magnet linked to a similar implanted magnet. Next, the electronics of the internal part are in charge (Figure 1). The signal is decoded into electric current in the implanted processor. Most implants use charge balanced biphasic current pulses with regulated amplitude, which are sent to a specific electrode contact. In present-day devices, the number of contacts varies between 12 -22. These contacts are situated on an electrode array, which usually is placed in the scala tympani and are distributed in this way along the cochlear duct such that each contact can stimulate a separate sub population of nerve fibers. The assumption is that due to the tonotopic order of the nerve fibers the patient experiences in this way a different sound percept. Here the apical part of the cochlea encodes low frequencies while the basal part encodes high frequencies.

Early start of electrical stimulation of the inner ear

Alessandro Volta (Figure 2), the inventor of the battery, was in 1790 the first to describe how electricity can be used to hear sounds (Volta 1800). He used two metal bars connected to a 50 volt battery and placed them in both ear canals. He perceived a “crackling and boiling” sensation, which can be compared with boiling soup. In the next century, Duchenne de Boulogne (1855), a neurologist who did pioneering work on muscular diseases, electro-diagnostics and electrical stimulation, realized that sound is a vibration. He used experiments with alternating current, where the patient perceived a sound comparable with the moving wings of a fly. In the 20th century the first implant was a fact. Andre Djourno and Charles Eyries (Djourno and Eyries 1957) implanted a self-made mono channel implant in a 50 years old patient, who became deaf after several ear surgeries on both sides. The implant had an external coil and an internal electrode, which was placed directly on the auditory nerve. The patient was able to detect noises, but speech recognition was impossible. The patient did, however, improve his lip-reading capabilities with the use of this implant.

Figure 2. *Alessandro Volta, 1745-1827*

This work was continued by an American otologist William House, together with a collaborating engineer Doyle in 1961. House implanted a new electrode array into the scala tympani. This array was designed to stimulate at five different places. However, the silicone of the array, which was used in these first implants, contained toxic substances and yielded rejection and explantation (Doyle et al. 1964). In 1968, William House continued his work on the cochlear implant and implanted a 5-channel array, which was changed later into a single electrode array, into several patients. House also produced in mid-1972 the first wearable speech processor with a speech coding strategy. Patients were not able to understand speech yet, but it was an addition to lip reading (House and Urban 1973).

In 1980 House developed the single-electrode 3M/House implant (Figure 3). In this implant the amplitude of an analog sound waveform was compressed and subsequently the amplitude was modulated to a 16-kHz sinusoidal carrier to serve as the effective electric stimulus. Only a few patients were able to obtain open-set speech understanding, which was not surprising given the limited spectral resolution. This single-channel stimulation did not make use of the tonotopic arrangement of the nerve fibers, unlike all modern multi-electrode implants have been developed to do. In 1984 the first multi-channel cochlear implant, developed by Graeme Clark, was launched on the market as the Nucleus Multi-channel Cochlear Implant. A study of 40 users showed significant and substantial improvement in speech reading, and in speech understanding with electrical stimulation alone (Dowell et al. 1986).

Figure 3. *The single-electrode 3M/House implant (1980); measuring 8.6 cm x 5.1 cm x 1.6 cm. This was the first cochlear implant approved by the FDA. It used a transmitter that had been worn just behind the ear, a microphone that had been pinned to the clothing and a body worn single channel speech processor.*

Speech processing strategies

The speech processor plays an important role in a cochlear implant. It is responsible for the extraction of specific acoustic features, after which the processor encodes these features via radio frequency transmission, and finally controls the parameters of electric stimulation.

Although a wide range of different speech processing strategies were developed over the last 30 years, they all make use of an implemented bank of filters to divide speech into different frequency bands. They differ, however, significantly in their processing strategies to extract, encode and transfer the right frequencies. The pathway towards used strategies nowadays is influenced by the processing capabilities of the original speech processors, insights in electrical stimulation and manufacturer's vision and implant design as will be described in the next section.

Spectral cues: Explicit feature extraction

The first multichannel Nucleus implant used a strategy, which was based on speech production and perception. The human ear is able to distinguish vowels from each other, because each vowels has a few fixed formants. A formant is a resonance on a certain frequency. Formants make an important contribution to the timbre of the voice and are also called the spectral peaks of the sound spectrum of the voice. Along this strategy spectral peaks of formants are extracted and delivered to different electrodes. The F0/F2 strategy (Clark et al. 1987; Seligman et al. 1984) was the first available strategy for the Nucleus wearable speech processor (WSP, (1982)) (Figure 4a). By using zero crossing detectors the fundamental frequency

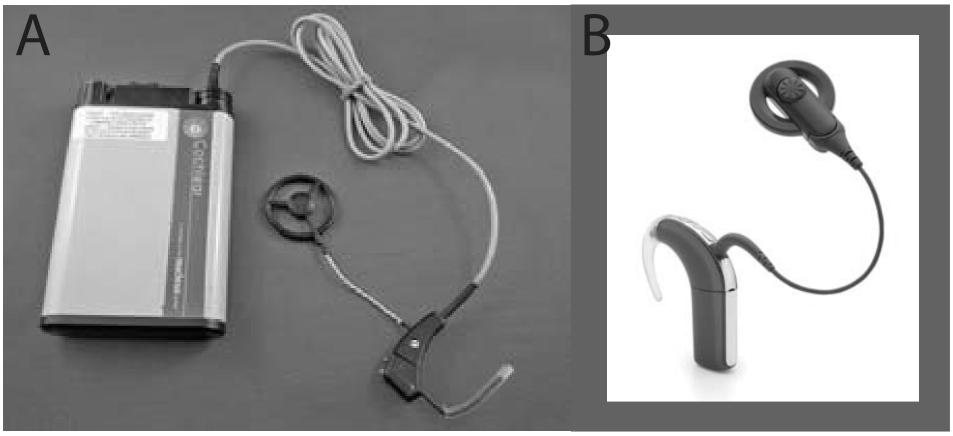

Figure 4. *(A) Wearable Speech Processor (1982); measuring 11.7 cm x 7.6 cm x 2.1 cm and weighing 255 gram with batteries; (B) CP810 (2012); measuring 5.1 cm x 0.9 cm x 1.9 mm and weighing 10.9 gram. Both are Nucleus® speech processors from Cochlear™, where (A) is the first processor, body worn and (B) is the most recent processor, worn behind the ear.*

F0, estimated from the output of a 270 Hz low-pass filter and the second formant (F2) estimated from the output of a 1000-4000 Hz band pass filter, have been extracted from the speech signal. The F0/F2 processor conveys F2 frequency information by stimulating the appropriate electrode in the 22-electrode array. Voicing information is conveyed with F0 by stimulating a selected electrode at a rate of F0 pulses per second. Initial results with the F0/F2 strategy were encouraging, because, as mentioned before, it enabled some patients to obtain open-set speech understanding (Dowell et al. 1986). In 1985 this strategy was modified to include information about the first formant frequency (F1), which resulted in the F0/F1/F2 strategy (Blamey et al. 1987). An additional zero-crossing detector was included to estimate F1 from the output. The processor selects two electrodes for stimulation, one corresponding to the F1 frequency, selected out of the first five apical electrodes, and one corresponding to the F2 frequency, selected out of the remaining 15 electrodes. The speech-recognition performance improved significantly by adding F1 information (Dowell et al. 1987; Tye-Murray et al. 1990). This was self-evident, given the importance of F1-F2 for normal-hearing listeners on speech recognition. However, it did not significantly improve on consonant-recognition scores. This is due to the fact that consonants do not have formants and that the F0/F1/F2 strategy emphasizes low-frequency information, which is required for vowel recognition. By including high-frequency information and spectral information in new hardware, Cochlear Limited improved the F0/F1/F2 strategy to the MPEAK strategy (Patrick and Clark 1991) in 1989 and this way improving the perception of consonants. Next, a new processor, the Miniature Speech Processor (MSP), was introduced, which used a custom integrated circuit for digital signal processing. In spite of large improvements in speech recognition (Dowell et al. 1991; Skinner et al. 1991), there were still several major limitations, including being the extraction of a speech signal embedded in noise.

Currently these speech specific feature extractions are not used any more in speech coding strategies.

Temporal cues

Compressed analog

Another line of strategy is the waveform strategy, which tries to present some type of waveform derived by filtering the speech signal into different frequency bands. An example of a waveform strategy is the compressed analog (CA) approach, which was first introduced in 1988 (Eddington 1980) and originally used in the Ineraid device. The Ineraid device used 6 active electrode contacts including two ground electrodes, which can be used as a reference electrode in monopolar stimulation. The device made use of monopolar stimulation and of percutaneous transmission. The CA approach is shown in Figure 5 in a block diagram. The acoustic signal is first compressed using an analog automatic gain control, because the amplitude levels or dynamic output range of the microphone do not match the dynamic input range

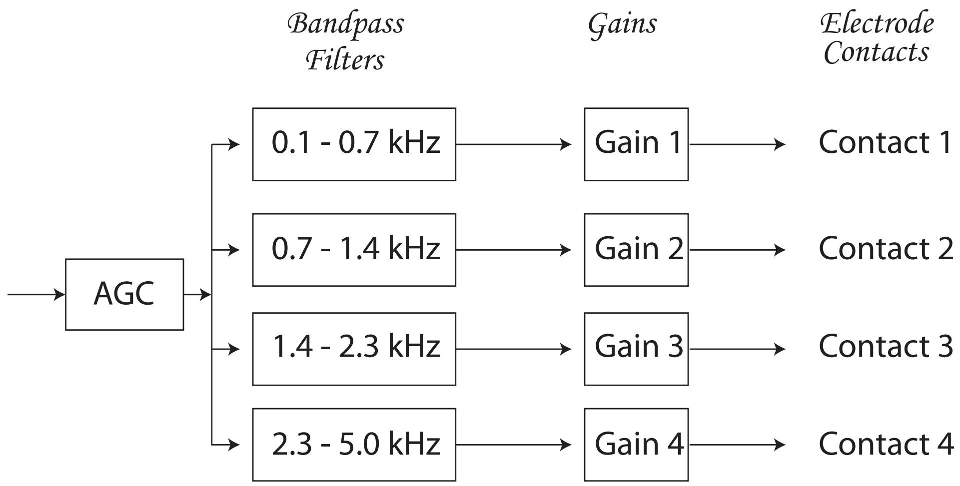

Figure 5. *Block diagram of the compressed analog (CA) approach used in the Ineraid device. The signal is first compressed using an automatic gain control. The compressed signal is then filtered into four frequency bands (with the indicated frequencies), amplified using adjustable gain controls, and then sent directly to four intra cochlear electrodes.*

of the processor. The compressed signal is then filtered into four consecutive frequency bands. In the next step the signal passes through adjustable gain controls and is sent directly to four intra cochlear electrode contacts. These waveforms are delivered simultaneously in an analog form. The electrodes operate in a monopolar configuration with the return electrode located outside the cochlea in the temporalis muscle.

The Clarion device (Advanced Bionics) (Schindler and Kessler 1992) made use of the compressed-analog processing in the Simultaneous-Analog-Strategy (SAS), which came on the market in 1996. One of the differences between CA and SAS is, is that CA is completely analog and SAS makes also use of digital signals. In the SAS mode, the acoustic signal is processed through eight filters, compressed and transferred simultaneously to eight electrode pairs. It makes use of bipolar electrode coupling in which each electrode is paired with another electrode that is proximate; the return electrode is in this case situated intra-cochlear.

Continuous interleaved sampling

The simultaneous stimulation appeared to be a problem for the CA approach due to a high interaction between channels caused by summation of electrical field from individual electrodes. With a Continuous Interleaved Sampling (CIS) approach, introduced in 1991 (Wilson et al. 1991), the channel interaction issue was addressed by using non-simultaneous interleaved pulses. Only one electrode has been stimulated at a time with this approach. The preprocessing is similar to the preprocessing of the CA processor, where the signal is first pre-emphasized, i.e. low-frequencies are attenuated and high frequencies amplified. Next, signals pass through a bank of band pass filters (Figure 6). The envelopes of the filtered waveforms are then extracted by full-wave rectification followed by low-pass filtering, i.e. low-frequencies pass through and higher frequencies are attenuated. Next the envelope outputs are compressed and used to modulate biphasic pulses.

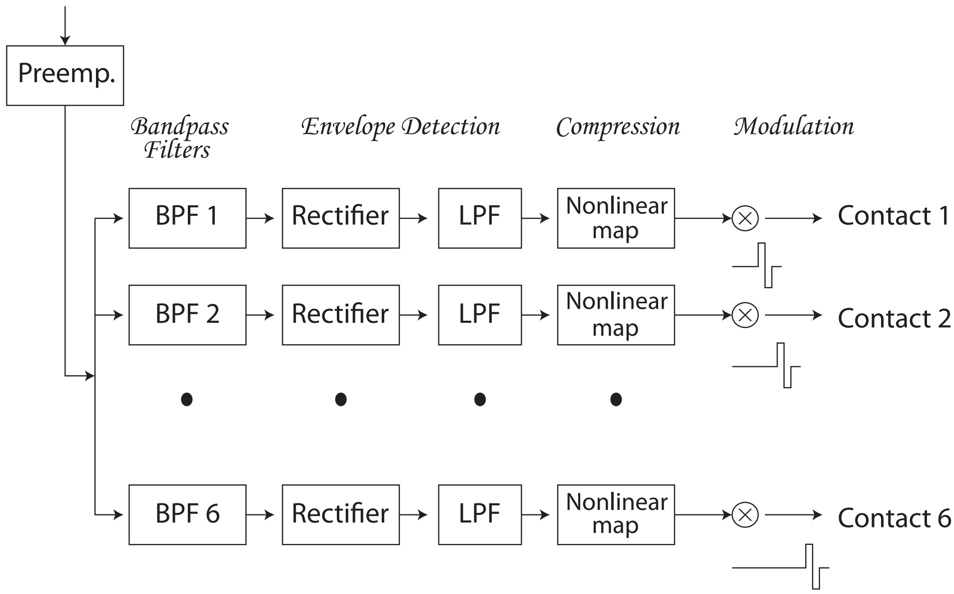

Figure 6. *Block diagram of the Continues Interleaved Sampling (CIS) strategy. The signal is first pre-emphasized and filtered into six frequency bands. The envelopes of the filtered waveforms are then extracted by full-wave rectification and low-pass filtering. The envelope outputs are compressed to fit the patient's dynamic range and then modulated with biphasic pulses. The biphasic pulses are transmitted to the electrodes in an interleaved fashion.*

A compression function is used to ensure that the envelope outputs fit the patient's dynamic range of electrically evoked hearing. In a typical CIS implementation, the number of band-pass filters is identical to the number of electrodes, ranging from 8 in the original Clarion CI device of Advanced Bionics (Figure 7a), to 12 in the Med El devices (Combi and Tempo) (Figure 8a) and 22 in the Nucleus devices. The HiRes strategy of Advanced Bionics is a close variation of CIS that uses relatively high rates of stimulation, relatively high cut-off frequencies for the envelope detectors, and up to 16 processing channels and corresponding stimulus sites.

With the development of CIS all the other strategies became superfluous, because of the large improvement in speech perception scores. Except for SAS, which still remained in use by Advanced Bionics next to CIS for several years, as some cochlear implant users performed better with SAS than with CIS (Battmer et al. 1999; Osberger and Fisher 1999; Stollwerck et al. 2001; Zwolan et al. 2005).

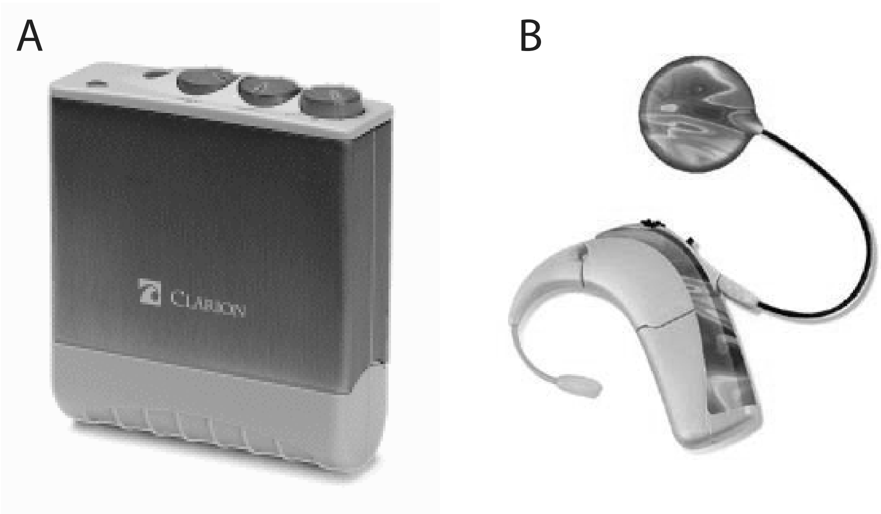

Figure 7. *(A) Clarion CI device (1996); (B) Harmony processor (2010). Both are processors from Advanced Bionics®, where (A) is their first processor, body worn and (B) is the most recent processor, worn behind the ear.*

"n-of-m"

Another variation on CIS is the "n-of-m" strategy (Wilson et al. 1988) were the number of physical contacts and filters (m) can be greater than the number of stimulating electrodes (n). In this strategy the envelopes of the n sub bands with the highest energy are selected to stimulate the corresponding electrodes. This strategy has been used in the Nucleus SPEAK (Spectra 22 (1995)) and ACE processor (Freedom (2005), behind the ear). The pre-processing is similar to the pre-processing of the CIS strategy, including the band pass filters and the envelope extraction blocks. A difference can be found in that the "n-of-m" strategy is based on temporal frames, whereas the CIS strategy does not have any explicit processing frames. Also, only the corresponding "n" electrodes out of the "m" electrodes are stimulated in a particular frame. The SPEAK strategy selects 6-8 largest peaks and has a fixed 250 Hz per channel rate. The ACE strategy has a larger range of peak selection and higher rate than the SPEAK strategy. If n=m, then SPEAK and ACE strategies are essentially the same as the CIS strategy.

A newer method is MP3000, which is a modification of the ACE strategy. This method uses a psychophysical masking model to select the amplitude components that are not masked by higher amplitude components and should be included in the signal. The other components are omitted from the transmission. This approach could improve spectral resolution. Four channels of this algorithm gave indeed a better performance with sentence-in-noise test (Buchner et al. 2008). The test with eight channels gave, however, comparable results.

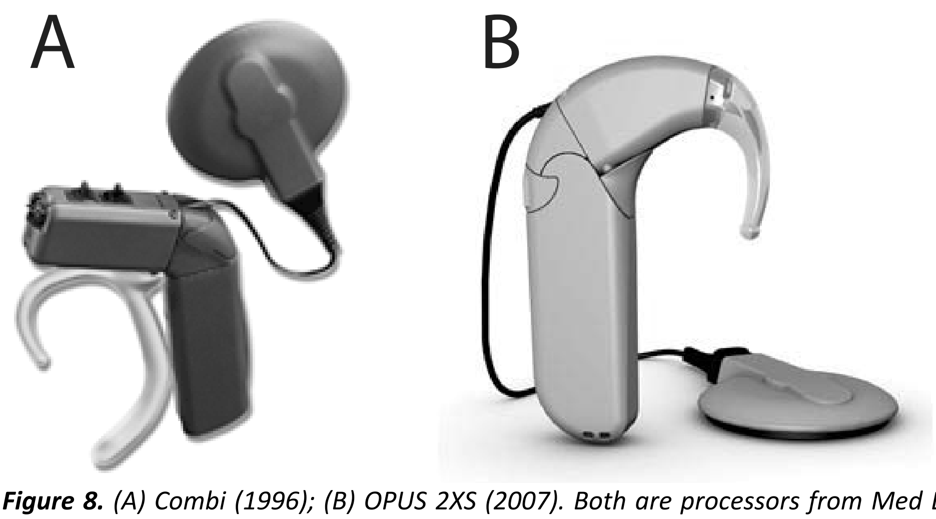

Figure 8. *(A) Combi (1996); (B) OPUS 2XS (2007). Both are processors from Med El and worn behind the ear.*

Fine features

The latest developments on speech processor strategies focus on how to encode spectral and temporal fine structure cues in cochlear implants, so speech recognition in noise and listening to music can be improved. In basic CIS like strategies, the fine timing or fine-structure of the sound waves are largely lost in the process from acoustic input to a fixed-rate sequence of biphasic electrical pulses. These implant users must rely on perceiving temporal envelopes (not temporal fine-structure) at specific places in the cochlea. Another problem is that with monopolar stimulation, which is used in these strategies, the place of excitation has not the desirable precision due to low spatial selectivity. For high levels of melody recognition, at least 64 individual channels are needed (Smith et al. 2002).

One way to encode the temporal fine structure is to increase the electric stimulation carrier rate so that the temporal fine structure cue can be represented in the waveform domain (e.g. Med El's FSP processor) (Figure 8b). Another approach is to represent the fine frequency information within bands using multiple sites of stimulation for each band and associated channel rather than the single site for each band and channel used in CIS and other strategies. This approach is a variation of HiRes (Advanced Bionics) and is called the HiRes with the Fidelity 120 option (HiRes 120) (Harmony processor) (Figure 7b). By stimulating two electrodes simultaneously, the number of discriminable sites is increased beyond the number of physical electrodes. This concept is called simultaneous dual electrode stimulation, current steering or virtual channels. In HiRes 120, 16 physical electrode contacts generate 8 intermediate pitches per electrode contact pair, giving a total of 120 different precepts. Unfortunately, no large improvements in speech perception are found with these fine feature speech processor strategies (Brendel et al. 2008; Buechner et al. 2008; Buechner et al. 2010; Donaldson et al. 2011; Firszt et al. 2009).

Another solution can be found in "conditioning" (Rubinstein et al. 1999). This processing is based on a physiological model. The auditory nerve in a normal-hearing ear has spontaneous activity effectively keeping the nerve ready to fire when an acoustic event activates it. The auditory nerve of a deaf ear lies dormant if it receives no input. Electrical stimulation of this last nerve leads to a high degree of synchrony firing across the spectrum, causing an extremely limited electrical dynamic range of about 10 to 30 dB. By using a "conditioner", a low-level, constant amplitude high-rate pulsatile stimulation, a pseudo spontaneous activity can be created and the dynamic range can be increased. This has been tried in a Conditioned CIS (CCIS) processing strategy, where a low-level conditioning stimulus at about 10 percent of the dynamic range has been combined with traditional CIS processing. The initial results of 30 subjects suggested better speech perception in noise for halve of the users and many implantees reported that music sounded better, but melody recognition showed no significant difference with CIS (Drennan and Rubinstein 2008). The implementation of CCIS is, however, limited because it can only be implemented on Advanced Bionics devices. This strategy has not made the transition from the academic trial to the clinic up till now.

Old methods brought into practice

Several methods to the improvement of speech perception with cochlear implants are under investigation at the moment. Of interest is that some of these methods were already known for several years, but due to technical limitations could not aptly be put into clinical practice.

Current steering, as mentioned in the previous paragraph, was first introduced by Townshend et al. (Townshend et al. 1987) in the late eighties to increase the number of distinct pitches a subject can discriminate. They showed that the perception of pitch can be varied between two adjacent electrodes by delivering the current simultaneously to both contacts. Recipients systematically reported a single-sound percept with a pitch that was between the base pitches of the individually stimulated contacts. This method was, however, not ready to be used in a speech coding strategy until recently (Brendel et al. 2008) in the Fidelity 120.

Another way to enhance the number of pitches is with phantom stimulation. This method had first been introduced by Wilson et al. (Wilson et al. 1993) in the early nineties to generate a pitch sensation lower than that produced by monopolar stimulation of the most apical electrode contact or higher than the most basal electrode contact. A phantom channel is a form of partial bipolar stimulation, with non-equal amplitudes out of phase on two adjacent stimulating electrode contacts, which results in that the excitation area is being pushed away from the stimulated contacts. This way the number of pitches can be enhanced beyond the electrode array. Saoji and Litvak (Saoji and Litvak 2010) showed in 2010 that it is possible to push the percept from 0.5 to 2 contact spacings away. After more fundamental research, one of the next steps is implementing this method in a speech coding strategy.

Large current spreads can impose limitations in cochlear implants and possibly degraded speech perception scores. Next to (partial) bipolar and (partial) tripolar stimulation, where two flanking electrode contacts are stimulated with non-equal amplitudes out of phase to reduce the region of excitation, Van Compernolle (van Compernolle 1985) suggested using all electrode contacts simultaneously (multipole stimulation) to reduce these effects of monopolar stimulation in the mid-eighties. This so-called phased array algorithm was validated by Van den Honert et al. (van den Honert and Kelsall 2007) in patients with respect to the electrode potentials in 2007 and the effect on neural excitation was investigated by Frijns et al. (2011) in a computational model of the cochlea in 2011. Before phased array channels can be implemented in a speech coding strategy, several issues remain to be addressed. For example, due to the focusing penalty, impractically high currents may be required to achieve sufficient loudness.

Overview of the present study

This thesis describes a translational study of dual electrode stimulation (DES), the stimulation type underlying Fidelity 120 and phantom stimulation as described above. The mechanisms of DES will be investigated both psychophysically and in a computational model of the cochlea, followed by a clinical implementation of DES to correct for defective electrode contacts.

There are different ways of stimulation. If the most apical electrode on an array is stimulated alone, we speak of Single Electrode Stimulation (SES) and subjects perceive a low pitch (Figure 9A). If the next electrode in the array is stimulated alone (SES), a higher pitch is perceived (Figure 9B). If these two electrodes are stimulated simultaneously with identical in-phase pulses, we speak of simultaneous Dual Electrode Stimulation (DES) or current steering; in this case the subject can perceive a pitch intermediate to the stimulated electrodes (Figure 9C). The current ratio divided over these two electrodes can change, expressed in percentages and each different percentage can give a different percept. Several studies showed that patients are able to discriminate different percepts with DES. However, not every patient is able to discriminate extra pitches, which suggest that these users may potentially not benefit from DES. Our objective is to establish how DES can be optimized and whether it has the same qualities as SES, enabling its use in a CIS like strategy. **Chapter 2** describes the comparison of DES with SES with respect to the site of stimulation in the cochlea, the spread of excitation (SOE) and sequential

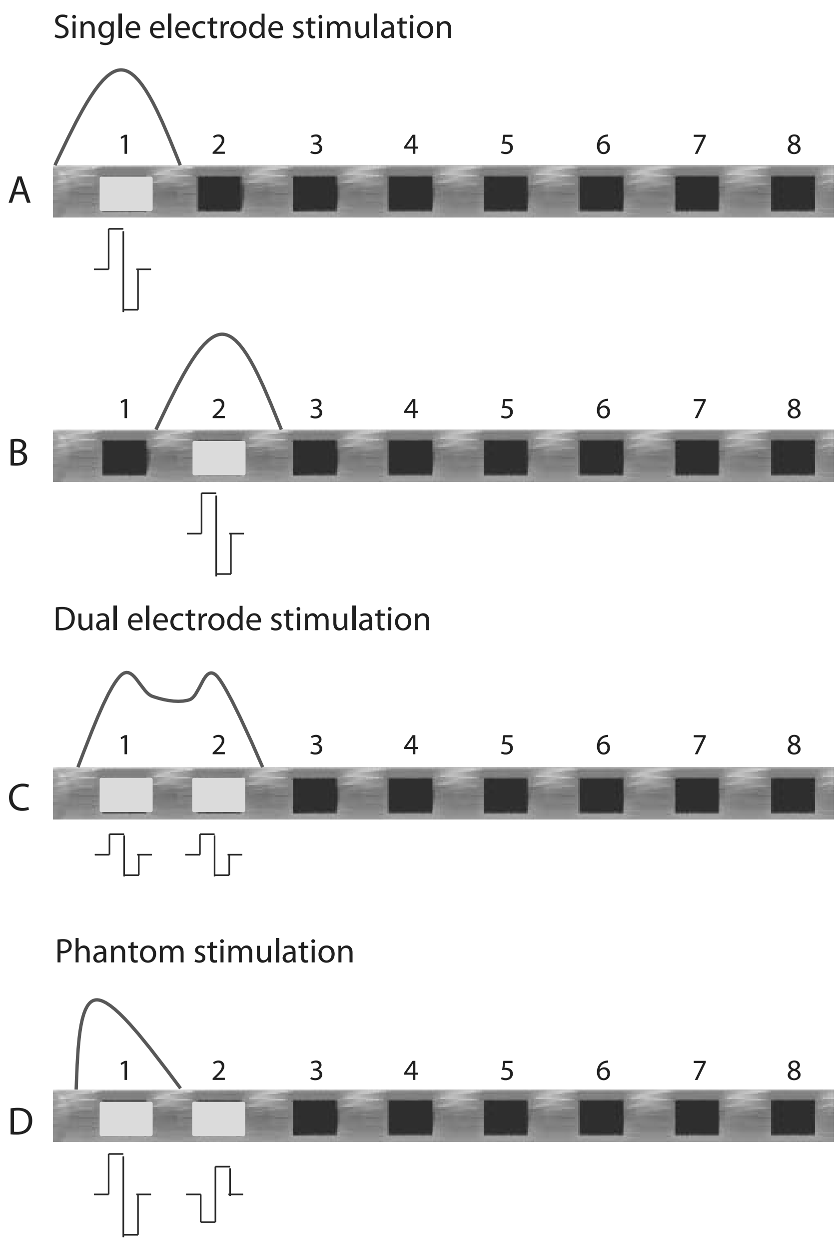

Figure 9. *Schematic illustration of single electrode stimulation on electrode contact 1 (A) and contact 2 (B), dual electrode stimulation (C) and phantom stimulation (D). The light gray electrode contacts are the stimulated contacts. The curve in each panel is hypothetical sketch of the place neural response. Condition is indicated by pulse waveform(s) beneath the stimulated contacts on the electrode array.*

channel interactions. It is of importance to be able to determine in advance whether a patient is able to discriminate extra pitches created with DES. It is investigated whether the number of intermediate pitches created with DES can be predicted from SOE, channel interaction measures, current distribution in the cochlea, or distance of the electrode to the medial wall.

DES can also be used to create a pitch beyond the electrode array in the apical region by using a pulse with opposite-polarity on the basal electrode contact of the pair (Figure 9D). It is called Phantom stimulation throughout this thesis. The pitch is than shifted away from the apical electrode and is lower in pitch than the pitch of the apical electrode contact with SES. The possibility for each patient to perceive a lower pitch with phantom stimulation is described in **chapter 3**. This phantom stimulation was further explored by using psychophysical experiments and computational modeling of the cochlea. It is investigated whether a current correction was necessary to maintain equal loudness effect and the place of stimulation was determined.

The last three chapters will further explore the possibilities and qualities of simultaneous DES. In **chapter 4** the possibility is explored to bridge defective electrode contacts with DES applied on non-adjacent electrode contacts. This type of DES is called spanning throughout this thesis. With psychophysical experiments spanning was compared with DES on adjacent electrode contacts in terms of the number of intermediate pitches, loudness effects and linearity of the current weighting coefficient with respect to the perceived pitch.

The experiments in all former chapters were performed on Most Comfortable Loudness (MCL) level. When DES will be used in a speech coding strategy, it is also of interest to know what happens at Threshold Level (TL), because of the clinical fitting procedure. TL is the level where the patient is asked to indicate when the signal was just heard. **Chapter 5** investigates the efficiency of DES at lower levels, with the focus on the requirements to correct for threshold variations. TLs were determined both psychophysically and with computational modeling, where the computational model utilized three different neural morphologies with different stages of degeneration.

After fundamental experiments with DES, the challenge remained if implementation of spanning in a speech coding strategy would be possible and would not decrease the performance and the quality of sound. In **chapter 6** three different speech coding strategies are designed, with 1, 2 or 3 defective electrode contacts next to each other. Each of the programs pretended to have a total of 6 defective electrodes. Patients were asked to use and evaluate these different strategies in home situation. Further, speech perception scores were measured in silence and with background noise.

An overall discussion of the major results and conclusions are presented in **chapter 7,** followed by some clinical implications and future perspectives.

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