Chapter 2

Integrated Use of Volume Conduction and Neural Models to Simulate the Response to Cochlear Implants

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Abstract

Cochlear implants are electronic devices intended to restore the sense of hearing in deaf people by direct electrical stimulation of the auditory nerve fibres that are still present in the deaf inner ear. Unfortunately, the clinical outcome is not very predictable. In this study a computational model is presented that can predict the neural response to an arbitrary cochlear implant. It first computes the potential distribution set up in a 3-dimensional, spiralling volume conduction model of the auditory part of the inner ear (cochlea) and then applies a nerve fibre model to construct input/output curves and excitation profiles of the auditory nerve. As an initial validation the results are compared with experimentally induced electrically evoked auditory brainstem responses. In the light of the favourable results, we conclude that the model can serve as a tool for designing future cochlear implants. In combination with electrophysiological measurements in the individual patient it is applicable as an implant fitting tool.
2.1 Introduction

In normal hearing, air pressure variations with frequencies between 20 Hz and 20 kHz are translated into neural information (action potentials) on the auditory nerve. This nerve conveys the information to the brainstem and higher auditory pathways. For this purpose the sound energy is picked up by the external ear and transmitted via the eardrum and the middle ear ossicles (malleus, incus and stapes) to the inner ear (cochlea). In the cochlea the final transduction from mechanical vibration into action potentials takes place. It is shaped as a tapered tube (the membranous labyrinth) that is wound in a spiralling fashion around the modiolus that contains the central axons of the auditory nerve fibres in their course to the brain stem. In humans the cochlea has 2 1/3 turns and is fully embedded in the solid petrous bone, while it has 3 1/2 turns and protrudes into the air-filled bulla (middle ear) in our experimental animal, the guinea pig. In physiological hearing the nerve fibres are arranged tonotopically, i.e. the nerve fibres located at the base of the cochlea (i.e. near the stapes) encode for the higher frequencies, whereas the more apical ones respond to the lower frequencies. In fact, the normal cochlea acts more or less as a mechanical Fourier analyser (Dallos et al., 1996), where each place along the basilar membrane (and thus each nerve fibre) is sharply tuned to respond to a specific frequency.

Hearing impairment, resulting from damage to the cochlea (usually to the outer or inner hair cells), is called sensorineural hearing loss. This induces elevated hearing thresholds and loss of tuning, resulting, e.g., in difficulties in understanding speech. Patients having mild to moderate sensorineural hearing loss can be helped with conventional hearing aids, which are basically sound amplifiers. In cases of profound sensorineural hearing loss (deafness) such conventional hearing aids are insufficient. For this group of patients cochlear implants have been developed. These are electronic devices that can give a sense of hearing to profoundly deaf patients by direct electrical stimulation of the spiral ganglion cells (primary auditory nerve fibres) that are still present in the damaged cochlea (Balkany, 1986). At present, over 16000 patients have been implanted world-wide with several devices of varying designs, most of which apply electrode arrays inserted into the scala tympani through the round window membrane at the basal end of it or through a so-called cochleostomy through the surrounding bone. In spite of promising results in approximately 25% of recently implanted patients, which are more or less able to take part in normal conversation without the help of lip reading, it is very difficult to identify the parameters that are crucial to predict the clinical outcome pre-operatively.
Figure 2.1: An artist’s impression of a Nucleus®-like cochlear implant inserted into the scala tympani of a guinea pig cochlea. The banded electrode array consists of Platinum contacts on a silastic carrier.
This outcome appears to be the result of a complex interplay between various patient and device related factors, which are not yet fully understood (Gantz et al., 1993). Initial research in this field was primarily defined in terms of clinical concerns. It established the feasibility of the approach and documented the beneficial effects and possible risks. However, in order to achieve a further improvement of the clinical results by more sophisticated implant designs, more information from basic research is needed to identify the key factors that need optimisation. Modern multichannel cochlear implants try to take advantage of the tonotopy in the cochlea by trying to stimulate localised sub-populations of nerve fibres by each electrode combination in the electrode array. The resulting configuration is illustrated in Fig. 2.1, which shows an artist's impression of a typical multichannel implant in a guinea pig cochlea. The spatial selectivity thus aimed at, is the electrical counterpart of the mechanical tuning, present in the normal cochlea.

This paper focuses on the development of a computational model of the implanted cochlea, which is intended to provide more insight in the fundamentals of functional electrical stimulation of the auditory nerve. This problem not only involves simulating the response of a nerve fibre to an externally applied potential field, but also the calculation of this potential distribution from the currents on the stimulating electrodes (Fig. 2.2). This is especially intricate in the case of cochlear implants due to the complex geometry of the inner ear. In previous studies we used a rotationally symmetric cochlear geometry to calculate neural excitation patterns and the spatial selectivity for different electrode configurations and stimulation patterns (Frijns et al., 1995; Frijns et al., 1996a). We showed that the simulation results were in good accordance with experimental data despite the use of a simplified geometry. In this paper, we will present and validate a more refined, helical representation of the cochlea. We will show how this model can be applied to give insight in the performance of various multichannel electrode designs.

### 2.2 Electrical volume conduction in the cochlea

Measurements of the in vivo electrical properties of a cochlea implanted with an electrode array confirmed that there is a strong influence of the cochlear electro-anatomy on the neural excitation patterns induced by cochlear implants (Black et al., 1983; Ifukube and White, 1987). An analytic solution of such a 3D volume conduction problem is restricted to geometries that are
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Figure 2.2: The conceptual framework behind the model of the electrically stimulated ear. The input signal is the current stimulus in the top-most panel, which is delivered by the speech processor. This current induces a potential field in the cochlea via the electrode system. This potential field, as computed by the volume conduction model, forms the input of the nerve fibre model that predicts which auditory nerve fibres will be excited. The information conveyed to the brain is characterised by the number, location and firing pattern of these fibres, the model’s output.
much simpler than the cochlea, and the first theoretical models on the (actually three-dimensional) potential pattern set up in the cochlea by the stimulating current sources assumed an exponential decay of current from its source to the nerve fibres along the cochlea, modelled in one dimension (O’Leary et al., 1985). Sapozhnikov (Sapozhnikov, 1990) computed potential distributions with a finite difference method in a linear, unrolled cochlear geometry, incorporating two cochlear turns. Girzon (Girzon, 1987) also used a finite difference method to compute the potential distribution in an anatomically-based three-dimensional volume conductor that included a continuously spiralling cochlear duct, and showed that the scala tympani acts in part as a terminated leaky transmission line. The limited spatial resolution of his model, however, did not permit the computation of neural excitation functions. Finley et al. (Finley et al., 1990) were the first to present an integrated three-dimensional neuron-field model of a segment of an unrolled cochlea, using the finite element method (FEM) and a passive nerve fibre model based upon activating functions (Rattay, 1993) for most of their computations. Suesserman and Spelman (Suesserman and Spelman, 1993) developed a so-called lumped-parameter model of the unrolled first turn of a guinea pig cochlea in which they incorporated resistive and capacitive components but did not include any neural element. Using the Boundary Element Method (BEM) (van Oosterom, 1991), we developed a rotationally symmetric volume conduction model of the second turn of the guinea pig cochlea, coupled with an active nerve fibre model (Frijns et al., 1995; Frijns et al., 1996a). Unlike the other models, the model preserved the contiguity in the modiolus of the auditory nerve fibres coming from different places in the cochlea. It was shown to give a more accurate description of the neural recruitment characteristics, especially for higher stimulus currents where excitation of nerve fibres in the modiolus takes place.

The BEM is also used in the present study, as it offers the advantages of a relative ease of mesh generation and the opportunity to perform calculations with multiple current source configurations instead of one, with a limited additional amount of computational effort. It requires discretisation of the boundaries between volumes with different conductivity rather than discretisation of these volumes themselves. To increase the numerical accuracy and to obtain a more realistic shape of the modelled cochlea we tessellated all boundaries with quadratically curved triangular surface elements on which the potential was also interpolated quadratically (Frijns et al., 2000b). The mesh was generated by spiralling the cross-section shown in Fig. 2.3 around the central axis the modiolus of and scaling it (Briaire and Frijns, 2000a). The resulting mesh is completely embedded in bone (the potential is defined to be 0 in infinity),
Figure 2.3: A Photomicrograph of the cross-section at the beginning of the second turn of a left guinea pig cochlea that was used to construct the boundary element mesh in (B). B. The modelled cross-section of the second turn of the guinea pig cochlea, showing how the contours of the cross-section in (A) can be represented adequately with parabolic line elements. The various compartments with different conductivities (see Table 2.1) are indicated (with BM=Basilar Membrane; SV=Stria Vascularis; OC=Organ of Corti) as well as the four electrode sites (A = near the outer wall; B = central in the scala tympani; C = near the spiral ganglion; and D = underneath the dendrites). The course of two nerve fibres, one ending in the modelled second turn and one in a more apical turn, is displayed.
and contains three turns (Fig. 2.4). It is locally refined in the vicinity of the current sources in order to minimise computational errors in regions of high potential gradients. The fact that the mesh does not include a helicotrema (the interconnection of the scala tympani and the scala vestibuli at the apex) is not expected to influence the results in this study since all current sources are placed at a relatively large distance from the apex.

![Figure 2.4: The 3D boundary element mesh of the cochlea used in the volume conduction calculations. It has local mesh refinements around the sites where the current sources are situated. In contrast to the in vivo situation the mesh spirals up to an apical closure point, so it does not have a so-called helicotrema where the scala tympani and scala vestibuli are interconnected.](image)

Table 2.1 illustrates the large differences in electrical conductivity between the various cochlear tissues: The fluid-filled scalae are highly conductive compared to the surrounding bone and membranes. In all simulations capacitive effects are neglected, as measurements have shown that this assumption is valid for frequencies up to 100 kHz (F. Spelman, personal communication).
Table 2.1: The conductivities of the various cochlear tissues as used in the computations (the data were compiled from Frijns et al. (1995)).

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Conductivity (Ωm)$^{-1}$</th>
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<tbody>
<tr>
<td>Scala tympani</td>
<td>1.43</td>
</tr>
<tr>
<td>Scala vestibuli</td>
<td>1.43</td>
</tr>
<tr>
<td>Scala media</td>
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</tr>
<tr>
<td>Stria vascularis</td>
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<tr>
<td>Reißner’s membrane</td>
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</tr>
<tr>
<td>Basilar membrane</td>
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</tr>
<tr>
<td>Organ of Corti</td>
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<tr>
<td>Bone</td>
<td>0.156</td>
</tr>
<tr>
<td>Nerve tissue</td>
<td>0.3</td>
</tr>
</tbody>
</table>

2.3 Simulating the auditory nerve fibre responses

Fig. 2.5A shows the anatomy of the primary auditory nerve fibres. These are thin bipolar nerve fibres, which are myelinated, i.e. the axon is covered by a highly insulating layer of Schwann cells. This layer is interrupted at more or less regularly spaced intervals, in the so-called nodes of Ranvier. In these nodes, the cell membrane contains voltage-dependent sodium and potassium channels that are responsible for the excitability of the nerve fibres. When elicited electrically, the action potentials propagate from node to node in both directions from their initiation point (so-called saltatory conduction) (Rattay, 1993). Basically, there exist two types of primary auditory nerve fibres. The majority are so-called high spontaneous rate (HSR) fibres, which have an axon diameter of 3 μm in guinea pigs and cats, while low spontaneous rate fibres have thinner peripheral processes (axon diameter 2 μm) (Gleich and Wilson, 1993; Liberman and Oliver, 1984). In a previous paper (Frijns et al., 1996a) we performed simulations with both types of fibres and concluded that these physiological variations in size of the auditory nerve fibres are not expected to have substantial influence on the performance after cochlear implantation. Therefore, we will here just perform calculations with a model equivalent of the HSR fibres.

In an attempt to model the behaviour of these fibres Colombo and Parkins (Colombo and Parkins, 1987) developed a model of the mammalian auditory-nerve neurone based on the classical work on amphibian nerve fibres of Frankenhæuser and Huxley (Frankenhæuser and Huxley, 1994). In order
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to fine tune the model to represent physiological data obtained from single auditory-nerve fibre experiments in squirrel monkeys they had to adapt the modelled nerve fibre’s anatomy significantly. Rattay and co-workers (Motz and Rattay, 1986; Rattay, 1993) used a single-node model to investigate the time structure of the response of the auditory nerve to electrical stimuli and concluded that the Hodgkin and Huxley (Hodgkin and Huxley, 1952) model of unmyelinated squid giant axon membrane simulates the electrically stimulated (myelinated!) auditory nerve best in time behaviour. We developed the so-called MSENN (Frijns and ten Kate, 1994) and SEF (Frijns et al., 1994) models which are non-linear cable models which represent essential mammalian nerve fibre properties, including spike conduction velocity, refractory behaviour and repetitive firing, better than previous models and can deal with arbitrary stimulus wave forms. The SEF model is based upon voltage clamp measurements in rat and cat motor nerve fibres at mammalian body temperature performed by Schwarz and Eikhof (Schwarz and Eikhof, 1987). In this paper, we will use a generalised version of the SEF model, which also describes the prolonged duration of action potentials and refractory periods in nerve fibres of smaller diameter like primary auditory nerve fibres (Fig. 2.5B) (Frijns et al., 1994; Frijns, 1995). The model treats the internodal myelin sheet as a perfect insulator, as it was in the original SEF model.

The simulations involved 365 nerve fibres, uniformly distributed along the three cochlear turns, each representing approximately 85 actual nerve fibres that are present in a real cochlear segment of $3^\circ$ ($\pm 0.6$ mm along the basilar membrane). To fit the nerve fibres into the tapered cochlea model we applied a linear scaling factor to the lengths of the three internodes of the peripheral process of the fibres in such a way that the relative position of the soma and the unmyelinated terminal to the membranous labyrinth was constant throughout the cochlea. This scaling factor ranged from 1.3 at the basal end of the cochlea to 0.43 at the apex, while it was 1.0 at the base of the second turn.

For each nerve fibre a system of 100 coupled non-linear differential equations (i.e. four equations for each of the 25 included active nodes of Ranvier) had to be solved. The details of the model equations and the parameters used are summarised in Appendix 2.A.
Figure 2.5: The form and function of the auditory nerve fibre model. Excitation of the fibre results in the production of an action potential (B) that is conducted to the brain along the axon. The electrical analogue of the mechanism in the so-called node of Ranvier that is responsible for the generation and propagation of the action potentials is shown in the lower left of (A).

2.4 Results

2.4.1 Potential distributions due to intra-cochlear electrodes

Fig. 2.6 shows the equipotential lines in a cross-section near the anode as computed for a longitudinal bipolar point current source of 1 mA (750 \( \mu \)m distance between the sources, called 'Bipolar+1', see below) at four representative positions in the scala tympani. It demonstrates the insulating effects of the highly resistive membranes surrounding the scala media, resulting in a relatively limited effect of the injected current on the nerve terminals in more apical turns. It is also clear that the potential distribution on the peripheral processes of fibres in the vicinity of the electrodes strongly depends upon the exact position of the electrode in the scala tympani. This is further illustrated in Fig. 2.7.
Figure 2.6: The potential distribution close to the anode due to a longitudinal current dipole (inter-electrode distance 750 μm) at four sites in the scala tympani, 1 1/3 turns from the basal end of the cochlea (A = near the outer wall; B = central in the scala tympani; C = near the spiral ganglion; and D = underneath the dendrites). The potentials are in mV for a 1mA source.
This figure shows for the electrode position in the centre of the scala tympani (B in Fig. 2.6) how the potentials vary along four representative nerve fibres, at the base, at the beginning of the second and the third turn and at the apex of the cochlea. It demonstrates that fibres in the implanted turn (1 in Fig. 2.7) experience the highest stimulating potentials in their peripheral process, and therefore they are most likely to be excited there. On the other hand, fibres from more apical turns (2 and 3 in Fig. 2.7) have their highest potentials in their modiolar part, i.e. where they pass by at the level of the electrodes. As contrasted with the widely spread concept based upon unrolled geometries (O’Leary et al., 1985; Suesserman and Spelman, 1993), this means that for the excitation of these fibres the current flow along the scala tympani (which would lead to elevated potentials at their peripheral processes) is less important than the current flowing directly into the modiolus. In other words, the electrode in the second turn will probably excite fibres originating in more apical turns in the modiolus rather than at their peripheral processes, giving rise to so-called ectopic or cross-turn stimulation (see below).

2.4.2 Model validation: the dependence of the neural responses on the electrode position

It was shown experimentally in cats that both the threshold currents and the slope of the input-output curves of the electrically evoked auditory brainstem response (EABR, an objective measure of the hearing sensation brought about by the electrical stimulus) depend upon the exact location of bipolar scala tympani electrodes (Shepherd et al., 1993). As these differences must be reflected in the excitation patterns of the auditory nerve at the level of the cochlea, these data are applicable to validate our model predictions against experimental results.

For this purpose we computed potential distributions in our volume conduction model of the cochlea for longitudinally directed bipolar electrodes at four locations (A=near the outer wall, B=in the middle of the scala tympani, C=adjacent to the modiolus and D=underneath the dendrites) comparable to the ones used experimentally (see Fig. 2.3B). We used the same biphasic current pulses (pulse width 200 μs/phase, the more apical electrode of the electrode pair acting as the cathode during the first stimulus phase) in our simulations as in the experiments, but all electrode spacings were scaled down by a factor 2 to account for the difference in size between the modelled guinea pig cochlea and the feline cochlea used in the experiments. For the so-called 'bipolar'
stimulus mode this resulted in a 375 $\mu$m inter-electrode distance, whereas it was 0.75 mm and 1.125 mm for the situations that will be referred to as ‘bipolar+1’ and ‘bipolar+2’, respectively (a terminology that was adopted from the Nucleus® cochlear implant that was used experimentally (Shepherd et al., 1993)).

![Graph](image)

Figure 2.7: The potential along the nerve fibres, at the base (0), at the beginning of the second (1) and the third (2) turn and at the apex (3) of the cochlea for electrode pair B in Fig. 2.6. The symbols indicate the position of the nodes of Ranvier. The cell body (soma) has a short length of 20 $\mu$m (see Fig. 2.5) and its position, which depends on the scaling of the peripheral process, can therefore be recognised by the two intersecting circles on each curve.

Using the potential distributions computed this way, we determined the excitation threshold for all 365 nerve fibres in the model, while we also recorded the node of Ranvier in which the initial excitation occurred. For the four ‘bipolar+1’ electrode configurations the results are presented as so-called threshold profiles in Fig. 2.8. For all four electrode pairs this figure shows a bimodal distribution of excitation thresholds in the vicinity of the implanted electrodes, and this pattern is repeated to some extent in the cochlear regions 1 turn more basal and 1 turn more apical than the stimulation current sources. This bimodality is a consequence of the fact that there is a zero-potential plane in between the
electrodes constituting the dipole and that the fibres run approximately parallel to this plane. The global threshold (defined as the level at which the first fibre starts firing) varies significantly among the four electrode positions, as we already expected from the potential distributions in Figs. 2.6 and 2.7.

The threshold profiles also show that above this global threshold there is a gradual spread of excitation around the site of current injection with increasing stimulus levels. This gradual recruitment of neurones is most likely to be perceived as an increasing loudness of the stimulus. At currents above $\pm 0.5$ mA (position C) to $\pm 1.7$ mA (position A) also fibres in higher cochlear turns are excited in the modiolus rather than at their peripheral processes. On the basis of the tonotopic organisation of the auditory nerve, this cross-turn stimulation, already alluded to above when describing Fig. 2.7, is expected to produce sensations corresponding with far lower frequencies than those associated with the place of the stimulating electrodes and therefore must be considered as an unwanted effect.

The data shown in a threshold profile can be summarised by plotting the number of excited nerve fibres as a function of stimulus level. This yields the so-called I/O-curves, shown in Fig. 2.9 for the same four 'bipolar+1' electrode configurations. In this plot, the excitation threshold is visible as the intersection of each curve with the abscissa. The slope of the I/O-curve is a measure of the spatial selectivity, since a steeper slope indicates that more fibres get excited with increasing stimulus levels. In accordance with this notion, the stimulus level at which cross-turn stimulation occurs can be recognised as a sudden increase of the slope of the I/O-curve.

From the results shown in Fig. 2.9 it is clear that -like in the experiments- also in the simulations both the excitation threshold and the slope of the I/O-curve depend upon the exact place of the electrode in the scala tympani. With other electrode spacings (375 $\mu$m = 'Bipolar' and 1125 $\mu$m = 'Bipolar+2') we found similar effects. The results are summarised and compared against Shepherd's experimental findings (Shepherd et al., 1993) in Table 2.2. It appears that the average ratio between the experimental and simulated current thresholds is approximately 3, rather than 1, which would obviously have been the ideal result. However, the fact that this ratio is fairly independent from electrode site and electrode spacing, implies that the model gives realistic predictions of the relative threshold shifts between the various electrode configurations. The main exception to this finding is the bipolar electrode in the C position, for which the ratio is even 6.6! This exception may be explained by the notion that the solution for this position is particularly sensitive to numerical limitations of

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Figure 2.8: Threshold profiles, showing the excitation thresholds of all fibres from the base (turn=0) to the apex (turn=3) of the cochlea for symmetric biphasic pulses with a duration of 200 $\mu$s/phase on so-called 'bipolar+1' electrode configurations (inter-electrode distance 750 $\mu$m) located 11/4 turns from the basal end of the cochlea. Stimuli were cathodic-first, which means that the more apical electrode acts as the cathode during the first stimulus phase. (A)-(D) indicate the same electrode pairs as used in Fig. 2.6.
Figure 2.9: I/O-curves, showing the percentage of nerve fibres that is excited as a function of the stimulus current (cathodic-first biphasic stimuli, 200 μs/phase). These data were computed from the threshold curves in Fig. 2.8.

the BEM method due to the close vicinity of 3 media with large steps in conductivity (nerve tissue, bone and perilymph). Other explanations of the discrepancies between the model and the experiments include the experimental uncertainty about the actual electrode positions and the biological variability between cats, clearly shown in Shepherd’s results. Furthermore, the anatomical differences between the cat cochlea and our guinea pig model are obvious, especially with respect to the exact location of the nerve fibres in relation to the medial wall of the scala tympani.

Table 2.2 also compares the slope of the I/O-curves (computed by counting the auditory nerve fibres that are excited 12 dB above the computed thresholds) against Shepherd’s data (Shepherd et al. (1993), Table V) on the slope of EABR I/O-curves. Ideally, the ratio between the EABR slope (in μV/dB) and the slope of the computed I/O-curve (expressed as the percentage of excited nerve fibres per dB) would have a constant value, as the relative contribution of each actual fibre to the amplitude of the EABR-response is believed to be constant. As shown in Table 2.2, this is largely the case for all 12 electrode configurations tested.

When comparing the results of these validation steps with those obtained with
Table 2.2: Comparison of the computed thresholds (Ith) and I/O-curve gradients for the first 12 dB above Ith (GIO, expressed as the percentage of modelled fibres that is excited) with corresponding experimental EABR data [28], Ithexp and GIOexp for all electrode spacings and electrode sites A-D. The values between brackets were computed with the omission of the data for the bipolar C position, which are most likely influenced by numerical errors (See text).

<table>
<thead>
<tr>
<th>Electrode Site</th>
<th>Ith</th>
<th>Ithexp</th>
<th>Ithexp/Ith</th>
<th>GIO</th>
<th>GIOexp</th>
<th>GIOexp/Ithexp</th>
</tr>
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<td>Bipolar</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>0.50</td>
<td>1.10</td>
<td>2.20</td>
<td>0.98</td>
<td>0.42</td>
<td>0.43</td>
</tr>
<tr>
<td>B</td>
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<td>0.99</td>
<td>3.67</td>
<td>0.73</td>
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<td>0.65</td>
</tr>
<tr>
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<td>0.66</td>
<td>6.60</td>
<td>0.66</td>
<td>0.33</td>
<td>0.50</td>
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<tr>
<td>D</td>
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<td>0.32</td>
<td>2.39</td>
<td>0.41</td>
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<td>0.51±0.10</td>
<td>(2.75±0.80)</td>
<td>(0.51±0.12)</td>
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</tbody>
</table>
As a test of the sensitivity of the model to uncertainties in the conductivity of the various media, we varied the individual conductivities up and down by a factor 2. It turned out that the changes to the computed neural excitation patterns were negligible for all media, except for perilymph and bone. The main effect of reducing the conductivity of the bone by 50% was an increase of the thresholds for ectopic stimulation by 1-3 dB depending on the electrode site. A decreased conductivity of the perilymph (comparable to fibrous tissue or bone formation in the scalae as quite often occurs after electrode insertion) results in an approximately proportionate decrease of the excitation thresholds, as well as a slight increase of the slope of the I/O-curves. As the conductivity of the perilymph is known within a few percent, and the conductivity of cochlear bone has been measured with an accuracy of approximately 30% (Suesser-man, 1992), we concluded that the model predictions are relatively insensitive to uncertainties in all conductivities.

2.4.3 Applications

All computations shown thus far involved point current sources. Actual cochlear implants, however, have electrode arrays with dimensions that are not negligible relative to the size of the scala tympani. As described in the companion paper (Briaire and Frijns, 2000a), the meshing software, developed to construct the mesh of the cochlea, also enables us to construct meshes of such clinically used electrodes. As these electrodes are intended to be inserted into the scala tympani without disruption of the cochlear tissues, the resulting situation can be modelled by simple addition of the meshes of the cochlea and the electrode. Then, the various electrode combinations can be simulated by the insertion of point current sources in the centres of the highly conducting ($\sigma = 10^7 (\Omega m)^{-1}$) areas representing the electrode contacts. Examples of such electrode meshes are shown in Fig. 2.10.

Preliminary simulations with a Nucleus®-like electrode (Figs. 2.1 and 2.10A) in the guinea-pig cochlea have shown results that are highly comparable with the ones shown in Table 2.2 provided that the cross-sectional area of the electrode is small ($< 10\%$, like in the clinical situation) relative to that of the scala tympani (Briaire and Frijns, 1998a). With bipolar stimulation thick electrodes result in reduced thresholds and current densities, while the spatial selectivity is comparable to that obtained with thin ones. The simulations also indicated that tripolar stimulation with this electrode is only favourable (i.e. highly selective) if it is thin, and that the associated high global excitation thresholds easily lead to high current densities at the electrode surfaces. This is an undesirable
Figure 2.10: Some examples of boundary element meshes of clinically applied electrodes. The black areas are Platinum surface contacts, the grey areas represent the silastic carrier. A. The Nucleus® electrode, the most commonly used electrode in clinical practice. It consists of 22 regularly spaced Platinum bands on a silastic carrier. B. The Clarion® electrode, which has 16 Platinum ball contacts (eight on the medial side, eight on top) that are partly recessed into the silastic carrier. C. The Clarion® Hi-Focus® electrode, which has 16 square Platinum contacts located medially, separated by silastic blebs, protruding from the carrier. It is intended to be displaced against the modiolar wall by a silastic positioner that is inserted laterally, against the outer wall.
condition, as electrical stimulation can lead to damage to biological tissues if the charge density per phase exceeds a certain critical level (Brummer and Turner, 1977).

Our group is especially interested in the use of extra-cochlear electrodes, which are placed in the bony labyrinth, just outside the cochlea. Such electrodes can be placed over the apex (the upper end of the cochlear spiral), which is inaccessible for scala tympani electrodes. This is particularly interesting in the light of the fact that many patients suffering from severe sensorineural hearing loss have relatively many intact auditory nerve fibres in this region. In addition, these low and middle frequency nerve fibres are important for the understanding of speech in normally hearing subjects, while these fibres also play an important role in directional hearing by detection of interaural time differences. An important drawback of the extra-cochlear location of electrodes is the fact that the distance between the stimulating electrodes and the excitable neural elements is relatively large. This is expected to result in higher stimulation thresholds and less selective stimulation. The higher stimulus currents involved may also impose limitations on the dynamic range, e.g., due to stimulation of the facial nerve. One of the ways we conceived to deal with the latter problem is to combine intra- and extra-cochlear electrodes as radial bipolar pairs. The fact that the electrodes are oriented radially eliminates the bimodal character seen in the threshold profiles for longitudinal dipoles (Fig. 2.8). In an earlier study (Frijns et al., 1996a) we demonstrated this for radially oriented scala tympani electrodes. We also found that the spatial selectivity with such electrodes can be higher than with longitudinal ones, but at the cost of a very limited range of useful stimulus levels since the threshold for cross-turn stimulation is very low. It is not surprising that with combined intra- and extra-cochlear ball electrodes similar effects are observed (Fig. 2.11A,C). The explanation for the relatively low thresholds for cross-turn stimulation follows from the potential distribution in the modiolus shown in Fig. 2.11A. The fibres from higher cochlear turns passing by in the modiolus, the leftmost part of the figure, will cross many equipotential lines. The main excitatory component for myelinated nerve fibres like these is the activating function (Rattay, 1993), i.e. the second order difference quotient of the nodal potentials to the place, and therefore this will result in a very large tendency of the fibres to start firing as soon as the stimulus current reaches even moderate levels. In this respect the situation in Fig. 2.11B is quite different. This figure displays the potential distribution set up by the same extra-cochlear ball electrode and an intra-cochlear wire electrode inserted over approximately the full length of the scala tympani, passing by through the centre of the ball electrode. In this case the
potential distribution around the extra-cochlear electrode is comparable to the one shown in Fig. 2.11, but the potentials in the modiolus are varying only very smoothly. In fact, the wire electrode acts more or less a Faradaic cage, protecting the modiolar parts of the fibres from being excited. The functional impact of this is reflected by the I/O-curves for both situations as depicted by Fig. 2.11, which shows that the introduction of the line electrode increases the useful range of stimulus levels (i.e. without cross-turn stimulation) to a large extent.

2.5 Conclusions and future directions

The method presented in this paper, which combines a helical 3D volume conduction model of the electrically implanted cochlea with an active neural excitation model, allows the prediction of excitation thresholds and spatial selectivity in cochlear implants. In accordance with electrophysiological experiments, it predicts that the excitation pattern depends on the exact location of the electrodes in the scala tympani (Frijns, 1995). These predictions are at least comparable with the ones obtained with a rotationally symmetric model, but the new geometry allows a wider variability of electrode geometries, including clinically applied designs like the ones shown in Fig. 2.10 to be included in the simulations. Therefore, the method is also applicable to develop and evaluate electrode configurations for future cochlear implant designs. An example of such a design, which we are currently evaluating in animal experiments in our laboratory, is the extra-cochlear ball vs. wire electrode demonstrated above (Fig. 2.11).

As there are large (size and shape) differences between the guinea pig cochlea and the human one, the next step in our project will be the construction of a mesh of the human cochlea. This not only will enable us to simulate human situations more realistically, but also will give us a tool to assess the validity of the (commonly carried out) extrapolation of data obtained in animal experiments to the clinical situation in humans. In doing so, one should be aware of the fact that -in contrast to all other species- in humans 90% of the cell bodies of the primary auditory nerve fibres are not myelinated. This means that human fibres carry an enlarged capacitive load which will have implications for excitation thresholds and spike timing, especially if degeneration of the peripheral processes due to prolonged deafness has occurred.

The results obtained thus far make us confident that this modelling approach
Figure 2.11: A. Potential distribution in a mid-modiolar cross-section in the vicinity of the electrodes, computed for the situation that an extra-cochlear electrode is stimulated against a ball electrode in the scala tympani (current strength 1 mA), in such a way that the electrodes form a radial bipolar pair. B. The same as (A), now with the scala tympani ball electrode replaced by a wire following the medial wall of the cochlea. C. I/O-curves computed for the situations in (A) and (B).
Appendix 2.A The generalised SEF auditory nerve fibre model

The auditory nerve fibre model used in the present paper (Fig. 2.5) is an active cable model of a guinea pig high spontaneous rate fibre, based on an extension of the SEF model (Frijns et al., 1994) to fibres of smaller diameter. Here we will only summarise the model equations and parameters of this auditory nerve fibre model. For symbols that are not explained in the text Table 2.3 will provide additional information. For further details we refer to the literature (Frijns et al., 1994; Schwarz and Eikhof, 1987). In Frijns et al. (1994) we showed that the model equations of a uniform finite-length active cable model with N nodes can be written as an equation with time-independent matrices A, B and C and time-dependent vectors describing the status of all nodes:

\[
\frac{d\vec{V}}{dt} = A\vec{V} + B\vec{V}_e + C \left[ \vec{I}_{act} + \vec{I}_L \right] 
\]

(2.A.1)

where: \(\vec{V} = (V_1, \ldots, V_N)\) - the deviation from the resting membrane potential, \(\vec{V}_e = (V_{e,1}, \ldots, V_{e,N})\) - the extracellular potentials due to the stimulating electrodes, \(\vec{I}_{act} = (I_{act,1}, \ldots, I_{act,N})\) - the sum of the active sodium and potassium current per node, and \(\vec{I}_L = -G_L V_L \cdot (1,\ldots,1)\) with \(G_L\) the nodal leak conductance, and \(V_L\) the leak current equilibrium potential.

For non-uniform fibres like the present auditory nerve fibre the structure of the matrices A, B and C given in Frijns et al. (1994) requires a slight modification, to account for the variation with segment number \(k\) of the nodal gap width \(l_k\), the internodal length \(L_k\) and axon diameter \(d_k\). This leads to the following dependence on \(k\) of the nodal membrane capacitance \(C_{m,k}\), the nodal leak conductance and the axoplasmic conductance \(G_{a,k}\):
Table 2.3: The parameters of the generalised SEF high spontaneous rate auditory nerve fibre model.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Unit</th>
<th>Symbol</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>axoplasm resistivity</td>
<td>Ω m</td>
<td>ρ_i</td>
<td>0.7</td>
</tr>
<tr>
<td>nodal membrane capacitance</td>
<td>pF</td>
<td>C_m</td>
<td>0.189</td>
</tr>
<tr>
<td>nodal leak conductance</td>
<td>nΩ⁻¹</td>
<td>G_L</td>
<td>2.43</td>
</tr>
<tr>
<td>nodal sodium permeability</td>
<td>(μm)³s⁻¹</td>
<td>P_Na</td>
<td>172</td>
</tr>
<tr>
<td>nodal potassium permeability</td>
<td>(μm)³s⁻¹</td>
<td>P_K</td>
<td>6.68</td>
</tr>
<tr>
<td>intracellular sodium concentration</td>
<td>mol m⁻³</td>
<td>[Na⁺]_i</td>
<td>10</td>
</tr>
<tr>
<td>extracellular sodium concentration</td>
<td>mol m⁻³</td>
<td>[Na⁺]_o</td>
<td>142</td>
</tr>
<tr>
<td>intracellular potassium concentration</td>
<td>mol m⁻³</td>
<td>[K⁺]_i</td>
<td>141</td>
</tr>
<tr>
<td>extracellular potassium concentration</td>
<td>mol m⁻³</td>
<td>[K⁺]_o</td>
<td>4.2</td>
</tr>
<tr>
<td>Temperature</td>
<td>K</td>
<td>T</td>
<td>310.15 ( = 37°C)</td>
</tr>
</tbody>
</table>

\[
G_L = \pi d_k l_k g_L, \quad (2.A.3)
\]

and

\[
G_{a,k} = \frac{\pi d_k^2}{4 \rho_i L_k}, \quad (2.A.4)
\]

where \( c_m \) is the membrane capacitance per unit area, \( g_L \) the leak conductance per unit area, and \( \rho_i \) is the axoplasm resistivity.

This results in the following expressions for \( A \), \( B \) and \( C \):

\[
A = \begin{pmatrix}
-G_{a,1} + G_{L,1} & G_{a,1} & \cdots \\
\cdots & \cdots & \cdots \\
-G_{a,k-1} + G_{L,k-1} + G_{a,k} & G_{a,k} & \cdots \\
\cdots & \cdots & \cdots \\
-G_{a,N-1} + G_{L,N-1} + G_{a,N} & G_{a,N} & \cdots \\
\cdots & \cdots & \cdots \\
\end{pmatrix} \begin{pmatrix}
\frac{C_{m,1}}{C_{m,1}} \\
\cdots \\
\frac{C_{m,k}}{C_{m,k}} \\
\cdots \\
\frac{C_{m,N}}{C_{m,N}} \\
\cdots \\
\end{pmatrix}
\]

\[
(2.A.5)
\]
\[
B = \begin{pmatrix}
-\frac{G_{a,1}}{C_{m,1}} & \frac{G_{a,1}}{C_{m,1}} & \cdots & \cdots & \frac{G_{a,k}}{C_{m,k}} & \frac{G_{a,k}}{C_{m,k}} & \cdots & \cdots & \frac{G_{a,N-1}}{C_{m,N}} & \frac{G_{a,N-1}}{C_{m,N}} \\
\vdots & \vdots & \ddots & \cdots & \vdots & \vdots & \cdots & \cdots & \vdots & \vdots \\
-\frac{G_{a,k-1}}{C_{m,k}} & -\frac{G_{a,k-1} + G_{a,k}}{C_{m,k}} & \cdots & \cdots & -\frac{G_{a,k}}{C_{m,k}} & -\frac{G_{a,k}}{C_{m,k}} & \cdots & \cdots & -\frac{G_{a,N-1}}{C_{m,N}} & -\frac{G_{a,N-1}}{C_{m,N}} \\
\end{pmatrix}, \quad (2.A.6)
\]

\[
C = \frac{1}{C_m} \begin{pmatrix}
1 & \cdots & 0 \\
\vdots & \ddots & \vdots \\
0 & \cdots & 1 \\
\end{pmatrix}. \quad (2.A.7)
\]

In the high spontaneous rate auditory nerve fibre model used in the present paper (Fig. 2.5) the nodal gap width \( l \) is fixed throughout the fibre. Also the axonal diameter \( d \) is identical on both sides of the cell body. The cell body itself has a larger internal diameter (10 \( \mu m \) instead of 3 \( \mu m \)). We could, however, not detect any influence of the soma thickness on the computed I/O-curves nor on the excitation profiles of the auditory nerve, but a large discontinuity in the axon diameter resulted in up to ten-fold increased computation times, due to the much smaller integration step-sizes required to maintain numerical stability. Therefore we decided to perform some of our computations with a 3 \( \mu m \) soma thickness.

The generalised SEF model equations describing the active nodal sodium and potassium currents \( I_{N_{a,k}} \) for each node \( k \) are:

\[
I_{N_{a,k}} = P_{N_{a,k}} n_k^2 h_k m_k^3 \frac{E_k F^2}{RT} \left[ \frac{[Na^+]_0 - [Na^+]_i}{1 - \exp(\frac{E_k F}{RT})} \right], \quad (2.A.8)
\]

\[
I_{K,k} = P_{K,k} n_k^2 \frac{E_k F^2}{RT} \left[ \frac{[K^+]_0 - [K^+]_i}{1 - \exp(\frac{E_k F}{RT})} \right], \quad (2.A.9)
\]
where $T$ is the absolute temperature, $F$ Faraday’s constant, $R$ the gas constant, $E_k$ is the transmembrane potential in node $k$, and $m_k$, $h_k$ and $n_k$ are dimensionless variables describing the kinetics of the ionic channels of node $k$. For $\vec{m} = (m_1, ..., m_N)$ the matrix-vector equation describing the set of first order differential equations that controls its time course reads:

$$\frac{d\vec{m}}{dt} = \begin{pmatrix} \alpha_{m,1} & \ldots & 0 \\ 0 & \ldots & \alpha_{m,N} + \beta_{m,N} \end{pmatrix} \cdot \vec{m}. \quad (2.A.10)$$

Similar equations apply for $\vec{h} = (h_1, ..., h_N)$ and $\vec{n} = (n_1, ..., n_N)$. The way the $\alpha$ and $\beta$ parameters in Eq. 2.A.10 depend on voltage and temperature is described in detail in our previous paper (Frijns et al., 1994). The equations are initialised with starting values $\vec{m}_0$, $\vec{h}_0$ and $\vec{n}_0$ respectively, that ensure that the nerve fibre is at rest at its resting potential $V_r$, i.e. $d\vec{m}/dt = d\vec{h}/dt = d\vec{n}/dt = 0$ at $\vec{V} = 0$. The value of $V_r$ is computed with the Goldman equation to account for variations in the ionic content of the extracellular medium:

$$V_r = \frac{RT}{F} \ln \left( \frac{P_{K}n_0^2[K^+]_0 + P_{Na}h_0m_0^3[Na^+]_0}{P_{K}n_i^2[K^+]_i + P_{Na}h_0m_i^3[Na^+]_i} \right). \quad (2.A.11)$$

In summary, for the 25 nodes of Ranvier included in the auditory nerve fibre model a system of 100 coupled non-linear first order differential equations had to be solved (viz. Eqs. 2.A.1 and 2.A.10 and the equivalent equations for and ). These equations were integrated by means of a fourth order Runge-Kutta algorithm with adaptive step-size control with step-sizes varying between 0.001 and 1s. These small integration steps were necessary because of the large range (over 40 dB) of stimulus strengths applied. As explained in Frijns and ten Kate (1994), a simple and robust threshold criterion is formed by the rise of the $m$ parameter (describing the sodium channel activation) above 0.7.