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Research Paper

A fast, stochastic, and adaptive model of auditory nerve responses to cochlear implant stimulation

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ABSTRACT

Cochlear implants (CIs) rehabilitate hearing impairment through direct electrical stimulation of the auditory nerve. New stimulation strategies can be evaluated using computational models. In this study, a computationally efficient model that accurately predicts auditory nerve responses to CI pulse train input was developed. A three-dimensional volume conduction and active nerve model developed at Leiden University Medical Center was extended with stochasticity, adaptation, and accommodation. This complete model includes spatial and temporal characteristics of both the cochlea and the auditory nerve. The model was validated by comparison with experimentally measured single fiber action potential responses to pulse trains published in the literature. The effects of pulse rate and pulse amplitude on spiking patterns were investigated. The modeled neural responses to CI stimulation were very similar to the single fiber action potential measurements in animal experiments. The model's responses to pulse train stimulation with respect to spatial location were also investigated. Adaptation was stronger at the borders of the stimulated area than in the center. By combining spatial details with long-term temporal components and a broad implementation of stochasticity a comprehensive model was developed that was validated for long duration electric stimulation of a wide range of pulse rates and amplitudes. The model can be used to evaluate auditory nerve responses to cochlear implant sound coding strategies.

1. Introduction

Cochlear implants (CIs) are implantable devices that partially restore auditory perception in individuals who have severe to profound hearing loss. CIs generally provide good speech understanding in quiet and have become the established mode of rehabilitation for adults with severe to profound hearing loss (Clark et al., 2013). However, CI users still experience difficulties understanding speech in noisy (real life) situations and suboptimal encoding of pitch accents due to limited transfer of the fine spectrotemporal details of the sound (Wouters et al., 2015). Many different sound-coding strategies have been introduced in the last decade to overcome this challenge, but no major advances have been made since the introduction of the Continuous Interleaved Sampling (CIS) strategy (Wilson et al., 1991; Zeng et al., 2008). New stimulation strategies are commonly investigated in psychophysical experiments and clinical trials, which is time-consuming for both the patient and researcher. Alternatively, strategies can be evaluated with the use of computational models. The present study presents a computationally efficient model that accurately predicts auditory nerve responses to arbitrary CI input signals.

A comprehensive computational model of the response of the auditory nerve to CI stimulation should include a realistic distribution of thresholds of all nerve fibers, and take into account both stochastic behavior and history effects. Stochasticity generally plays a role in the human sensory system (Verveen and Derksen, 1968) and is present in the auditory nerve's responses to electrical stimulation (Rubinstein, 1995). Animal experiments have demonstrated variance in neural responses to different pulses in a pulse train (Bruce et al., 1999a, 1999b; Dynes and Delgutte, 1992; Miller et al., 1999; Shepherd and Javel, 1997). In addition, animal experiments (Cartee et al., 2000; Litvak et al., 2001; Miller et al., 2008; Zhang et al., 2007) have shown a dependency of auditory nerve

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Abbreviations: SFAP, Single Fiber Action Potential; CIS, Continuous Interleaved Sampling; CI, Cochlear Implant; RS, Relative Spread; eCAP, electrically evoked Compound Action Potential; ARP, Absolute Refractory Period; RRP, Relative Refractory Period; SD, Standard Deviation; PSTH, Post Stimulus Time Histogram; IH, Interval Histogram; pps, pulses per second

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behavior on previous neural spikes and pulses, referred to as the history effects. Here, history effects include refractoriness, facilitation, adaptation, and accommodation. Refractoriness is the diminished excitability of the nerve immediately following an action potential. Facilitation is a threshold decrease caused by a preceding sub-threshold pulse. Adaptation refers to a threshold increase caused by long-term firing of the neuron. Accommodation refers to a threshold increase caused by a long-term stimulation current and occurs when the membrane slowly depolarizes due to the stimulus. Accommodation and adaptation recently received increased attention as important aspects in neural responses to long duration electrical stimulation (Hay-McCutcheon et al., 2005; Hughes et al., 2012; Liu and Wang, 2001; Negm and Bruce, 2014, 2008; Woo et al., 2009; Woo et al., 2010). Neural adaptation, a decrease in neural excitability during persistent stimulation, is important for efficient coding of dynamically varying inputs (Bohte, 2012; Drew and Abbott, 2006; Zilany and Carney, 2010). Although some early research was equivocal about the existence of auditory nerve adaptation in response to electrical stimulation (Parkins, 1989), several reports indicate that electrical stimulation leads to adaptation of the auditory nerve (Javel et al., 1987; van den Honert and Stypulkowski, 1987). Several groups have investigated the effects of long duration continuous or pulsatile electrical stimulation on nerve activation based on single fiber action potential (SFAP) measurements of the auditory nerve (Dynes and Delgutte, 1992; Hartmann et al., 1984; Javel et al., 1987; Shepherd and Javel, 1997; van den Honert and Stypulkowski, 1987). In order to predict the performance of patients with CIs in discrimination tasks, the complete nerve fiber's response has to be predicted. A complete cochlear model is required to investigate the responses of the auditory nerve in both the spatial and temporal domain. A model of the whole nerve is needed to investigate the influence of the spatial location of auditory nerve fibers on temporal response patterns.

Different types of models are available to predict nerve responses to electrical stimulation. A major distinction can be made between the biophysical and phenomenological type of models. Biophysical models quantitatively describe nerve membrane behavior in response to an induced membrane current and have been shown to correctly predict membrane responses to single pulses and reasonably predict latencies, refraction, and facilitation effects (Frijns et al., 1994; Frijns and ten Kate, 1994; Reilly et al., 1985; Schwarz and Eikhof, 1987). These models can be combined with 3D volume conduction models of the cochlea to predict auditory nerve responses to electrical pulses as reported by Kalkman et al. (2015). Biophysical model parameters are based on patch-clamp single fiber recordings, from which high order effects, required to model responses to long duration pulse trains, are difficult to obtain. In addition, the calculation of responses to long duration pulse trains using these models requires long computational times. Phenomenological models directly relate empirical observations to expected neural output. Such models have been used to efficiently predict responses to sustained stimulation by direct implementation of stochastic and temporal behavior (Bruce et al., 1999a, 1999b; Chen and Zhang, 2007; Litvak et al., 2003; Macherey et al., 2007; Stocks et al., 2002; Xu and Collins, 2007). All proposed phenomenological approaches modeled auditory nerve fibers as single nodes and incorporated at most 20,000 fibers. The models that included a geometric current spread all modeled the electrode contacts as point sources located in homogeneous media. Phenomenological models that simulate thresholds are only capable of dealing with pre-defined pulse shapes.

The goal of the current study was to develop a hybrid model that incorporates spatial and pulse-shape effects from a biophysical model, as well as temporal effects and stochastic responses from a phenomenological model. The model had to be computationally efficient in order to predict whole nerve responses to long duration pulse trains. By merging the biophysical and phenomenological approaches in a compound model, we utilized the merits of both methods and minimized their disadvantages. The model was validated by comparison with experimentally measured SFAP responses to pulse trains published in the literature. The model's output with regards to discharge rate, rate variances, rate decreases, and pulse intervals was evaluated for pulse trains with different rates and amplitudes. For clarity the comparison between model predictions and animal data from the literature will be given directly in the results section. In the discussion section the similarities and differences between predictions and data will be interpreted and analyzed in terms of model parameters.

2. Materials and methods

2.1. Model

The model presented in this paper builds on the previously published 3D volume conduction model of the cochlea and deterministic cable model of the human auditory nerve (Kalkman et al., 2015). The cochlear geometry is based on micro-CT data, the electrode array geometry is based on the HiFocus1J, modelled in lateral position. The model presented in this paper extends the deterministic thresholds from active GSEF nerve fibers (Briaire and Frijns, 2005; Frijns et al., 2000) with stochastic behavior and history effects (Fig. 3). Deterministic thresholds are obtained at 3200 spatially different locations using the 3D volume conduction model, an overview of the model is shown in Fig. 1; for details of its implementation we refer to Kalkman et al. (2015). At each of these locations, 10 different nerve fibers are modeled. Thus, the model of the whole auditory nerve effectively incorporates a total of 32,000 different auditory nerve fibers. The deterministic thresholds of the 3D model are used as input to the phenomenological model extension; only the thresholds of entire fibers are taken into account, and not the individual thresholds of each Ranvier node. For each nerve fiber, stochasticity is induced by adding a relative spread (RS) to the deterministic thresholds. To account for refractoriness these stochastic thresholds are elevated depending on the time since the last spike relative to refractory period. Spike adaptation

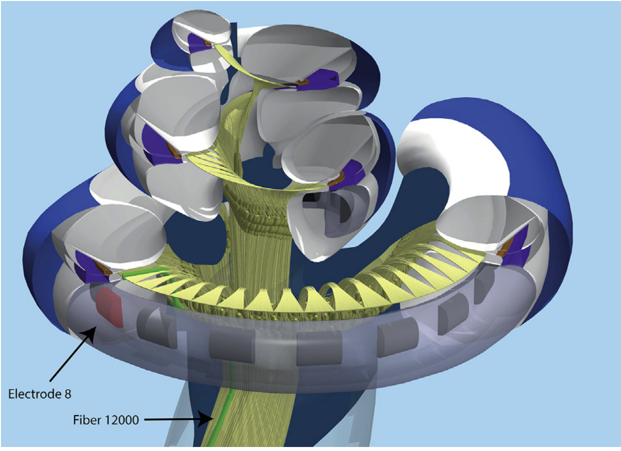

Fig. 1. 3D model overview. Unless stated otherwise, the simulations were done by stimulating the electrode located at roughly 175° from the round window, here highlighted in red. Most of the simulations were done on fiber 12000 (fiber 1200 in the 3D model), here highlighted in green; fibers are counted from basal to apical cochlear locations. The tip of this fiber is located roughly at the same cochlear angle as the stimulated electrode. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)