Modeling pulse train stimulation of electrically stimulated auditory nerve fibers

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Introduction

Auditory nerve fibers (ANFs) encode the synaptic input from the inner hair cells into afferent spiking information that is thereafter processed by the different nuclei in the auditory system. If the hair cells in the inner ear are degenerated and therefore not able to provide synaptic input to ANFs, cochlear implants (CIs) can be used to stimulate the ANFs (spiral ganglion cells) directly with electrical pulses. Such an electrical stimulation provides hearing for profoundly deaf people, often restoring the ability to understand speech in quiet conditions. However, researchers and device manufacturers are still searching for the optimal coding strategy that would improve the ability of CI users to cope in complex listening environments with multiple sound sources.

The coding-strategy optimization process could benefit from computational models that are able to predict peripheral responses evoked by different stimulation patterns. To that end, we have developed a phenomenological model for the ANF response to arbitrary pulse shapes and sequences. It is adapted from the model by Horne et al. [1], which can reproduce physiological data from single pulse stimulations. We have developed that model further to account for inter-pulse interactions in pulse train stimulation. Here, we show that our revised model is capable of reproducing data from studies involving pulse train stimulations.

Method – modeling principles

The model consists of two leaky integrate-and-fire (LIF) model units that are thought to correspond roughly to the *peripheral* and *central* part of the neuron. Both LIF models are sensitive to different polarities in biphasic pulses. Further, the membrane potential from the ¨peripheral¨ unit is thought to travel to the ¨central¨ unit. Apart from this, the two units are considered to be independent and able to generate action potentials at different time instants. If one or both of the units is to generate a spike, a principle of *first-come, first-serve* is emulated, allowing the earlier spike to be considered in the spike train output of the model. That spike also launches the simulation of refractory and recovery behavior of the ANF that prevents a potentially later-arriving spike from the other unit to pass during the absolute refractory period of the neuron. The refractory behavior is emulated by momentarily increasing the threshold values, making it harder for subsequent pulses to evoke spikes. The following sections aim to describe the processes in more detailed manner.

From electrical pulse to action potential

The action-potential-generation process is modeled identically as in [1] based on the LIF principle. That is, the auditory nerve fiber is thought to integrate incoming electrical current and to release an action potential if the membrane voltage exceeds a stochastic threshold and if the neuron is not hyperpolarized before it is ready to spike. In the model, this principle is simulated by first processing the pulsatile input signal with a first-order low-pass filter to obtain an estimate for the membrane potential as a function of time. The next step comprises searching for the time instant at which the membrane potential exceeds the stochastic and time-varying threshold value. This threshold crossing launches the action-potential-generation process that emulates a stochastic delay [2] In the model by Horne et al. [1]], this process is divided into two steps: an *initiation* step and a *generation* step. The *initiation* step has a stochastic duration and it needs to be finished before the end of a critical period, otherwise no spike is generated. The critical period is defined as the time from the threshold crossing to the time when the neuron is hyperpolarized by the second phase of a biphasic pulse. If the *initiation* step is completed in time, a spike is generated but a stochastic delay is introduced between the threshold crossing and the time of spiking to account for the latency and jitter of the ANF [1, 2].

Refractory and recovery behavior of ANF

In all sensory neurons, generation of an action potential is followed by an absolute refractory period during which the neuron cannot be excited to generate another action potential. After the absolute refractory period greater-than-normal membrane voltage is required to excite the neuron while the neuron gradually recovers to the resting state.

Here, we follow the traditional approach and set the threshold level to an infinite value during the absolute refractory period and multiply the threshold value with an exponentially decaying function to simulate the relative refractory period. We use the same equation for the exponential function that was used by Hamacher [3]. Hence, upon spiking, the threshold values of the ¨peripheral¨ and ¨central¨ units are multiplied with the function

$$f(t) = \begin{cases} \infty & , t < t_{\mathrm{ARP}} \\ \left[\left(1 - \exp\left(\frac{-t + t_{\mathrm{ARP}}}{0.1 t_{\mathrm{RRP}}}\right)\right) \dots \right. \\ \left. \left(1 - 0.68 \exp\left(\frac{-t + t_{\mathrm{ARP}}}{0.1 t_{\mathrm{RRP}}}\right)\right) \right]^{-1} & , t \geq t_{\mathrm{ARP}}. \end{cases}$$

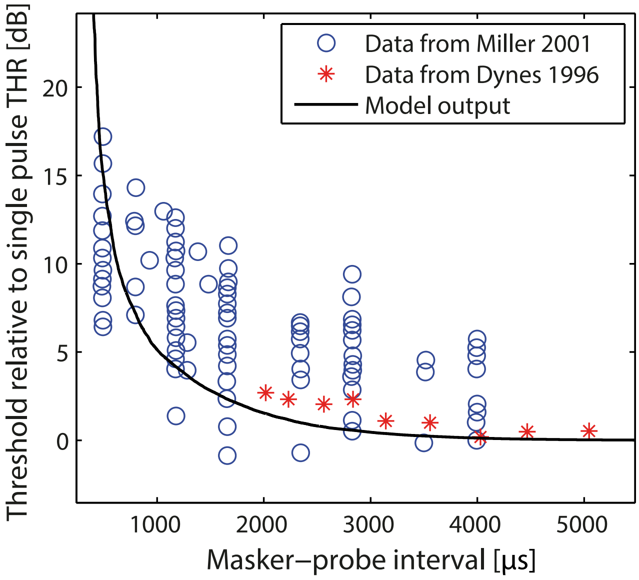

Figure 1: Results for modeling refractoriness of the auditory nerve fiber. The model output follows the trend in the neurophysiological data [4, 5].

Here, t is the time from last spiking and $t_{\mathrm{ARP}}$and t_{RRP} denote the absolute and relative refractory periods, respectively. However, we introduce stochasticity to the absolute and relative refractory times to account for the found variation in the neurophysiological data [4, 5]. Specifically, the absolute and relative refractory times of each neuron are thought to be exponentially distributed having expected values of 0.6 and 1.2 ms as well as minimum durations of 0.3 and 0.6 ms, respectively.

Results

The response of an auditory nerve fiber to pulse train stimulation is influenced by several phenomena. Specifically, refractoriness, facilitation, accommodation, and spike-rate adaptation phenomena affect which of the pulses are able to excite the neuron (see, [6] for a review). Here, we inspected how well our model can account for the refractoriness and spike-rate adaptation aspects using neurophysiological data from literature.

Modeling refractoriness

To evaluate refractory behavior we compared our model output against the neurophysiological data from Dynes [4] and Miller et al. [5]. Both of these neurophysiological experiments employed a masker-probe pulse paradigm where a supra-threshold masker pulse is being followed by a probe pulse after a specific inter-pulse interval. The level of the probe pulse is adjusted to the threshold level at which spikes are recorded for both the masker and the probe. The results shown in Fig. 1 illustrate that the model output is well in line with the neurophysiological data.

Modeling spike-rate adaptation

Spike-rate adaptation can be thought as the neuron's approach to save energy and to avoid encoding of redundant information by adapting its response to a continuous, time-invariant stimulus. It can be observed, e.g. by inspecting the spike timings in the form of an inter-spike-interval (ISI) histogram. One aspect of spike-rate adaptation is best observed at low pulse rates such as 250 pulses/s. At such a low pulse rate one could expect the neuron to fire with equal probability for every spike since the inter-pulse-interval is longer than the recovery time of the neuron. However, as shown in Fig. 2(a), the measured [7] and predicted ISI histograms show peaks also at integer multiples of the inter-pulse-interval. In other words, spike-rate adaptation can be observed in the neuron's resistance to spike for every pulse in the sequence.

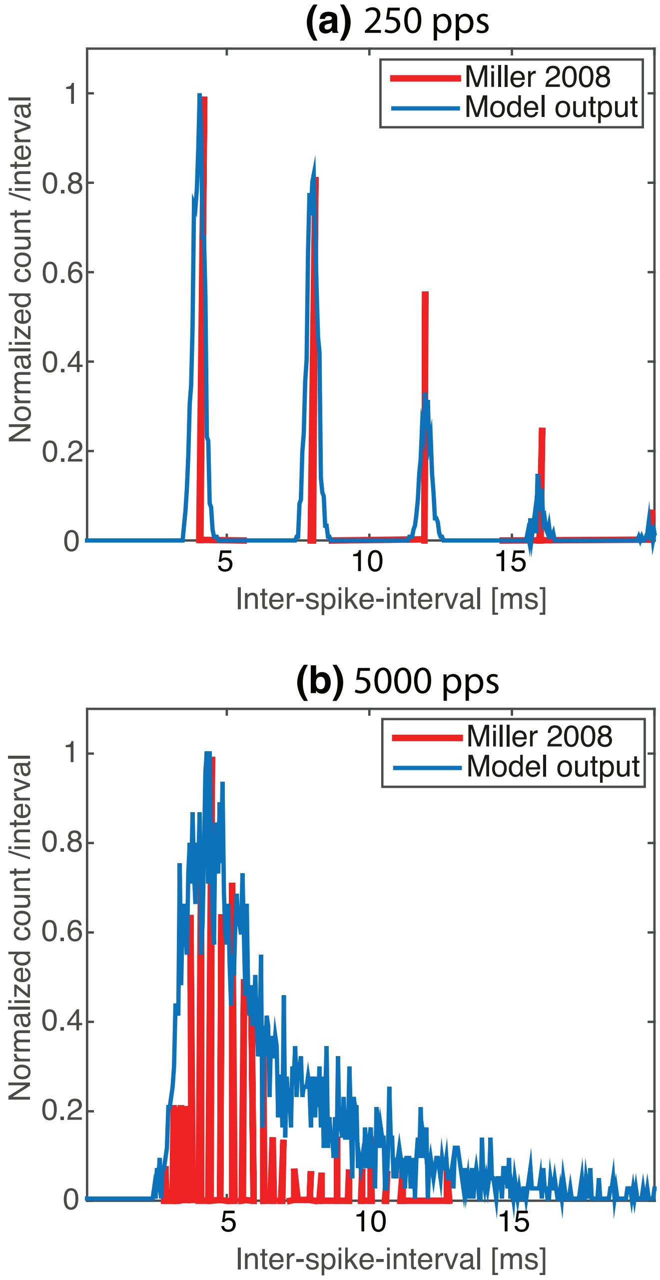

Figure 2: Results for modeling spike-rate adaptation. The model output demonstrates the pulse-rate dependency of the spiking intervals [7].

At high pulse rates such as 5000 pulses/s, the ANF cannot spike for every stimulating pulse in the sequence due to the refractoriness phenomenon. In addition, facilitation enables consecutive pulses to jointly excite the neuron and the accommodation phenomenon reduces the neuron's likelihood of spiking after several pulses have failed to excite it. As a consequence, the ISI histogram does no longer exhibit peak(s) at location(s) corresponding to the pulse rate, but a stochastic distribution centered on the interval corresponding to the neuron's preferred spiking rate. Figure 2(b) shows that the model output is able to demonstrate this aspect of pulse-rate adaptation as well.

Summary

In this article, we presented a phenomenological model for the electrically stimulated auditory nerve fiber (ANF). It builds on the model by Horne et al. [1] which we have extended for pulse train stimulation. Specifically, elements modeling the recovery and refractory behavior of ANF were added and the model was extended to include two integrator units corresponding roughly to the peripheral and central part of the neuron. The revised model was shown to be able to account for the neurophysiological data about refractoriness phenomenon and to demonstrate aspects of spike-rate adaptation phenomenon.

Acknowledgements

Supported by Bernstein Center for Computational Neuroscience, Munich (BMBF 01 GQ 1004B).

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