



Modeling auditory-nerve responses to electrical stimulation

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Publication date:
2014

Document Version
Publisher's PDF, also known as Version of record

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Citation (APA):
Joshi, S. N., Dau, T., & Epp, B. (2014). *Modeling auditory-nerve responses to electrical stimulation*. Poster session presented at 7th Forum Acusticum, Krakow, Poland.

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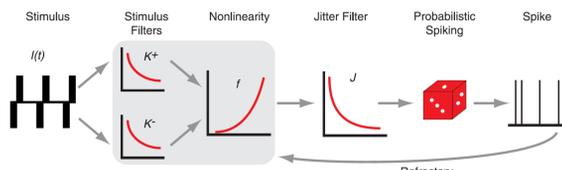
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Introduction

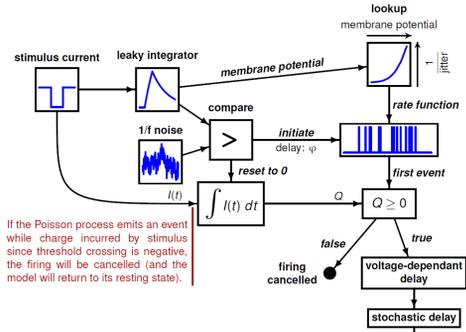
Cochlear implants (CI) directly stimulate the auditory nerve (AN), bypassing the mechano-electrical transduction in the inner ear. Trains of biphasic, charge-balanced pulses (anodic and cathodic) are used as stimuli to avoid damage of the tissue. **The pulses of either polarity are capable of producing action potentials (AP) whereby the sites of initiation of the AP differ for the two polarities.** A cathodic pulse triggers an AP in the peripheral axon, whereas an anodic pulse triggers an AP in the central axon. **The latency difference between the APs initiated at the different sites is about 200 μs ,** which is large enough to affect the temporal coding of sounds and hence, potentially, the communication abilities of the CI listener. In the present study, **two recently proposed models of electric stimulation of the AN [1,2] were considered in terms of their efficacy to predict the spike timing for anodic and cathodic stimulation of the AN of cat [3]. The models' responses to the electrical pulses of various shapes [4,5,6] were also analyzed.** It was found that, while the models can account for the firing rates in response to various biphasic pulse shapes, **they fail to correctly describe the timing of AP in response to monophasic pulses.** Strategies for improving the model performance with respect to correct AP timing are discussed.

Methods

Two models are simulated with single pulses of various shapes (monophasic, biphasic and pseudomonophasic) with a sampling frequency of 1 MHz. Both models are parameterized with a chronaxie value of 276 μs . Each model is simulated 1000 times for each pulse level to obtain probability of response.



Goldwyn's point process neuron [1] is parameterized based on point process theory with five parameters reported from the single neuron recordings, namely Threshold, Relative spread, Chronaxie, Jitter and Summation time constant. Model includes a low-pass filter characterizing the neural membrane and nonlinear stages that add noise and produce an output spike.



Horne's model [2] falls under a family of leaky integrate-and-fire neuron model and is been modified to include stochastic delays to produce appropriate spike latencies.

Results

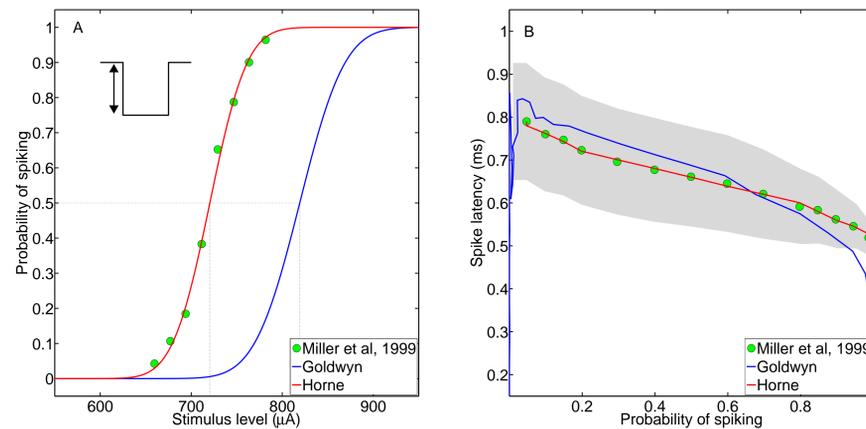


Fig 1 Probability of firing a spike with increase in stimulus level, known as the firing efficiency (FE) curve, for stimulation with monophasic cathodic pulse of 39 μs with cathodic pulses is shown along with model responses in **Fig 1 A**. Data is shown in green circles, predictions of Goldwyn's model in blue and of Horne's model in red. Both models can reproduce the FE curves with accuracy. Average spike latencies and its jitter (standard dev. of spike latencies) for monophasic cathodic pulses is plotted as function of probability of spiking in **Fig 1 B**. Both models can predict reduction in spike latencies with increase in level.

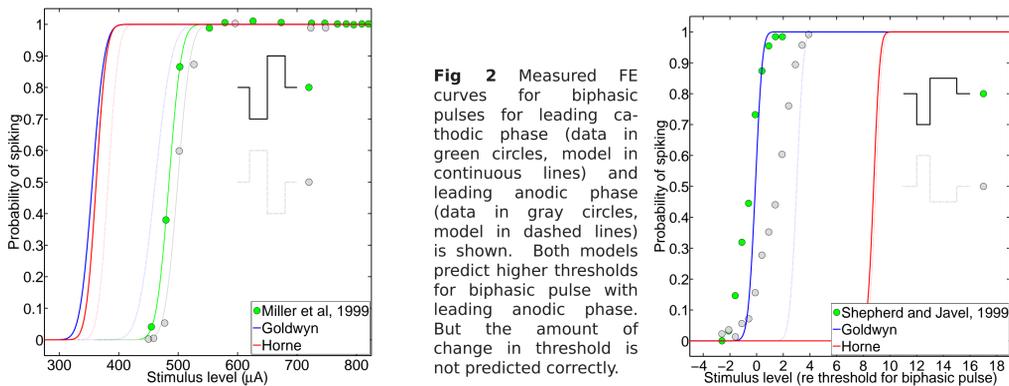


Fig 2 Measured FE curves for biphasic pulses for leading cathodic phase (data in green circles, model in continuous lines) and leading anodic phase (data in gray circles, model in dashed lines) is shown. Both models predict higher thresholds for biphasic pulse with leading anodic phase. But the amount of change in threshold is not predicted correctly.

Fig 3 Responses to stimulation with pseudomonophasic pulses when excitatory phase is cathodic (PSC, data in green circles, model responses in continuous lines) and when it is anodic (PSA, data in gray circles, model responses in dotted lines). The thresholds are normalized in respect to threshold for biphasic pulse (cathodic first). Both models predict increased thresholds for PSA, but fail to correctly predict the threshold.

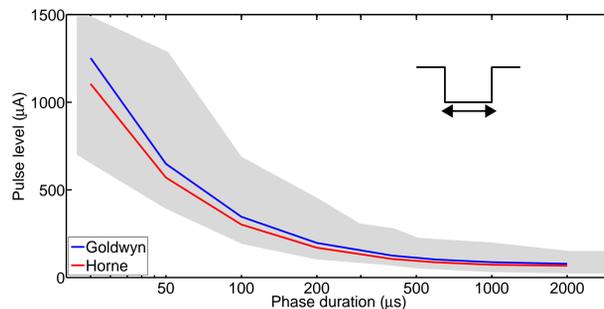


Fig 4 Variability across neurons in strength-duration curves for monophasic cathodic pulses measured in [5], in gray area. Both models produce similar strength-duration curves (lines), depicting correct responsiveness to monophasic cathodic phase stimulation.

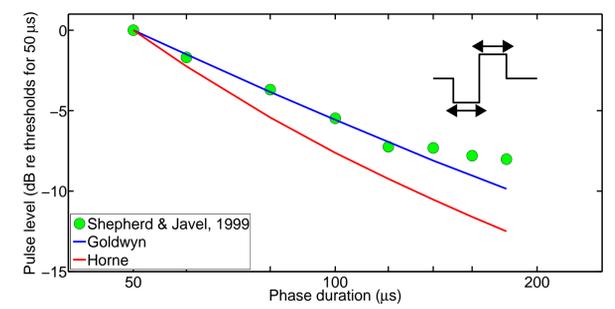


Fig 5 Data (green circles) and model predictions (lines) of thresholds for symmetric biphasic pulses as function of phase duration is shown. The data is normalized with respect to threshold for biphasic pulse of 50 μs . Goldwyn's model predicts the effect of phase duration with more accuracy than Horne's model.

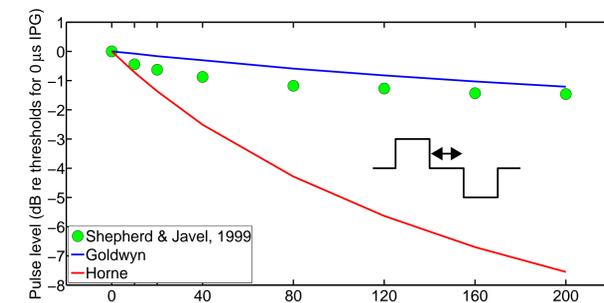


Fig 6 Data (green circles) and model predictions (lines) of threshold for biphasic pulses of 100 μs as function of the inter-phase gap (IPG) are presented. Thresholds are normalized with respect to threshold for pulse with IPG of 0 μs . Both models fail to predict the effect of IPG on threshold.

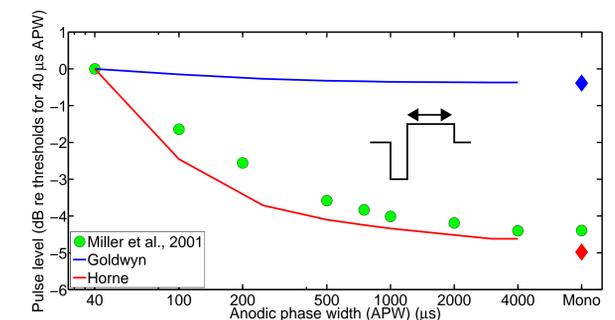
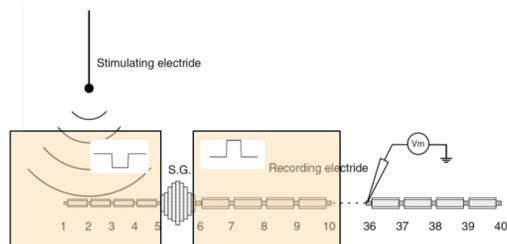


Fig 7 Data (green circles) and model predictions (lines) for biphasic pulses as function of the duration on anodic phase are shown. Horne's model predicts the effect of anodic phase duration with more accuracy than Goldwyn's model.

Discussion



An illustration of electrical stimulation with cochlear implant and setup of experiment for single neuron recording adopted from Kumsa and Mino (2013).

- Based on latencies of the spikes produced by monophasic pulses, it is believed that each phase excites a different site of excitation
- Both the models are responsive to cathodic phase only and can reproduce the single neuron data for cathodic stimulation
- Both models also fail to reproduce effect of inter-phase gap and pulse phase duration on thresholds
- This failure is attributed to the lack of responsiveness to anodic phase
- Lack of single neuron data available to understand the mechanisms responsiveness of the auditory nerve to electrical stimulation limits the formation of efficient models

Conclusion

- State-of-the-art models of electrical stimulation of auditory nerve fail to reproduce responses to stimulation with various pulse shapes
- A neuron model that can correctly reproduce responses to various pulse shapes can be useful to understand the properties of information coded in the auditory nerve through electrical stimulation and to objectively evaluate the stimulation strategies
- Development of such a model requires understanding responsiveness to monophasic pulses as well as interaction between the two polarities

Acknowledgement: Authors would like to thank Colin Horne for sharing a code of his model. The work has been funded by grant from the People Programme (Marie Curie Actions) of the European Union's 7th Framework Programme FP7/2007-2013/ under REA grant agreement number PITN-GA-2012-317521.

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