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A model of auditory nerve responses to electrical stimulation

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Model Structure

This study introduces a phenomenological model of the AN cell for electrical stimulation. The model consists of two exponential integrate-and-fire type point-neurons, representing peripheral and central nodes of the AN cell. A cathodic pulse depolarizes the 'peripheral' neuron and anodic pulse depolarizes the 'central' neuron. Both the neurons simultaneously, but independently, integrate the electric charge imposed by the stimulus. A first spike produced by either neuron pushes the model to the absolute refractory period, during which no spike can be fired. Both the 'peripheral' and the 'central' neurons are parametrized based only with responses to monophasic stimulation in cat AN. The model is tested for it's ability to predict responses to various pulse shapes.

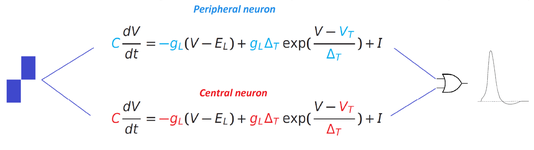

Fig.1 Schematics of the AN model for electrical stimulation with 'peripheral' and 'central' neuron. The membrane potential of each neuron is calculated using the differential equations shown above, where V is the membrane potential, C is the membrane capacitance, g_L is the membrane conductance, Δ_T is the exponential slope factor, V_t is the threshold, and is the leak reversal potential. The parameters that differ between the two neurons have been highlighted by color.

The neural membrane is a leaky-integrator of the electrical charge and is characterized by deriving the strength-duration relationship. In this framework, stimulus level required for a pulse of infinite duration is defined as the **rheobase**, and defines the leakage characteristics of the neural membrane. The duration at which the level required to evoke a spike is double the rheobase is defined as the **chronaxie**.

The values of rheobase and chronaxie are derived from fitting a curve to the strength-duration data with a function, Q = rheobase (t + τ). A relationship between threshold and inverse of the pulse duration is linear (Nowak and Bullier, 1998). In a linear regression line fitted to these data, the absolute of y-intercept of the line equal to the rheobase current and slope of the line is a product of the chronaxie and rheobase.

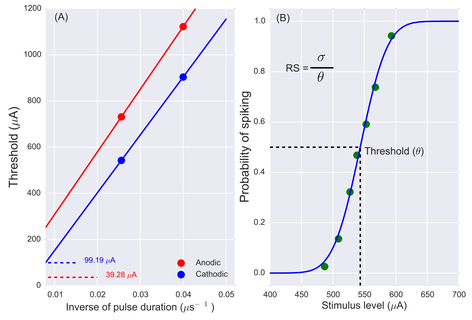

Fig.2 (A) Mean thresholds for 26 and 39 μS monophasic pulses reported in Miller et al. 1999 are used to obtain the rheobase and chronaxie values for both, the anodic and cathodic stimulation. The dotted lines show absolute values the y-intercept (interpreted as the rheobase) for the line fit to the data. Chronaxies for anodic and cathodic stimulation are 821.42 and 246.35 μs, respectively. **(B)** An illustration of the firing efficiency (FE) curve obtained, by calculating the probability of spiking for a given stimulus level. Threshold is defined as the level at which probability of spiking is 0.5. Relative spread is a measure of the dynamic range of the neuron, and is obtained by dividing the standard deviation of the integrated Gaussian fitted to the FE curve by threshold of the neuron.

Finally, the model also includes a noise source that is required to produce probabilistic spiking behaviour observed in neurons. The noise used here is of $1/f^{\alpha}$ type noise which has been shown to correctly predict the membrane voltage fluctuations in neural membranes.

Parametrization

- Chronaxie and Rheobase is obtained from data on monophasic stimulation from Miller et al. 1999 (Shown in Fig.2 (A)).
- The membrance resistance is calculated using rheobase.
- The membrane capacitance is calculated using chronaxie and the membrane resistance.
- The standard deviation of the noise distribution is calculated using relative spread (RS) and thresholds reported in Miller et al. 1999.
- Value of α is adjusted to predict the correct RS for monophasic stimulation.
- Δ_T is adjusted to predict correct spike latencies for monophasic pulses, as reported in Miller et al. 1999.

Monophasic stimulation

The model is evaluated for stimulation with monophasic and charge-balanced biphasic pulses of various shapes. Model is run at the sampling rate of 10^6, and probabilities are obtained by running the model 10000 times at each stimulus level.

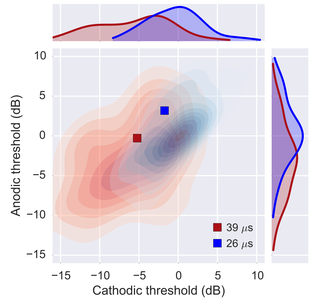

Fig.3 Thresholds predicted by the model for monophasic anodic and cathodic pulses, for two durations. The density kernels show the corresponding data from Miller et al. 1999. The thresholds are presented as dB re 1mA.

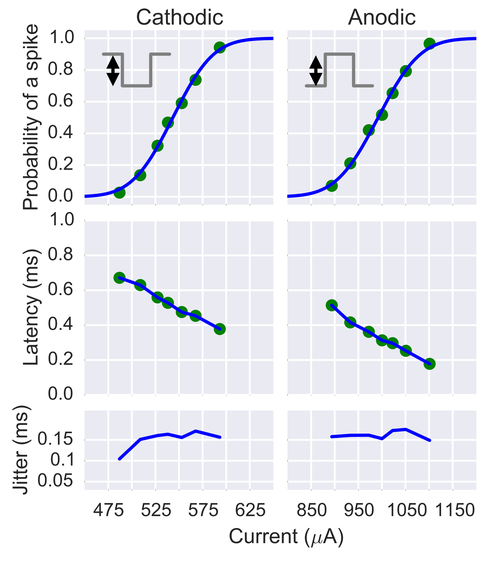

Fig.4 The firing efficiency curves, spike latencies, and jitter observed in model responses to stimulation with monophasic cathodic and anodic pulse of 39 μs duration. Model can correctly predict the latency and threshold difference between anodic and cathodic pulses reported by Miller et al. 1999. Value of jitter, however, does not decrease with increase in level and the FE, as it does in data.

Biphasic stimulation

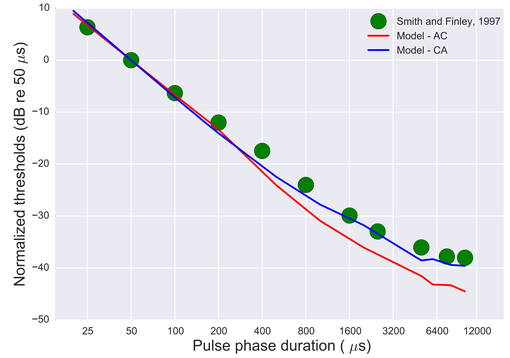

Fig.5 Data and corresponding model responses to change in threshold of cats to monopolar stimulation with biphasic pulses (anodic-cathodic). Model predicts large differences between anodic-cathodic and cathodic-anodic pulses at higher pulse durations.

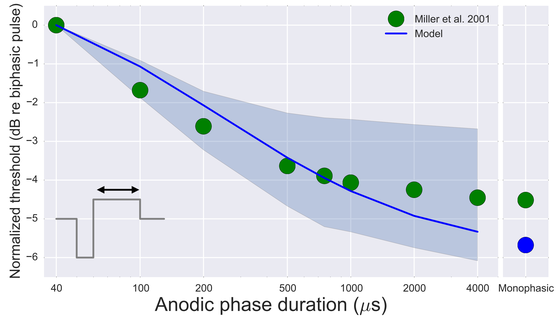

Fig.6 Thresholds for charge balanced biphasic (cathodic-anodic) pulses with varying anodic phase duration. The data and model predictions have been normalized re threshold for symmetric biphasic pulse. The model can predict the trend of decreasing threshold with increase in anodic phase duration.

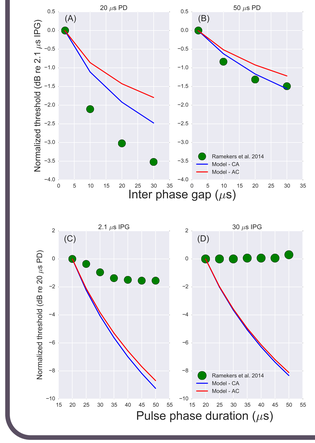

Fig.7 Interaction between inter-phase gap (IPG) and pulse-phase duration (PPD). The threshold data is derived from ECAPs recorded rom guinea pigs implanted with CI. While the model can qualitatively predict the effect of IPG at two different PPDs (A), it overestimates the effect of PPD at a given IPG (B). Whether these differences are due to the different animal model, or because of differences in ECAP and single neuron responses is unclear.

Further Evaluation

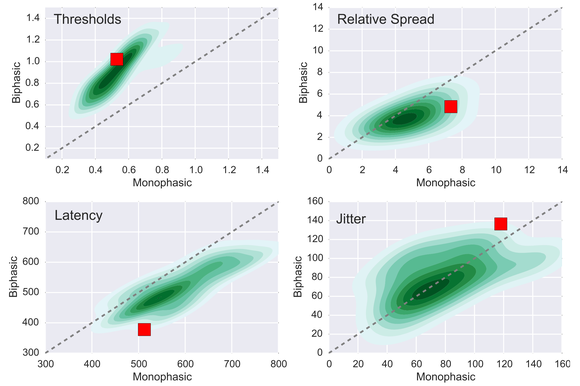

Fig.8 Miller et al. 2001 presented comparison of response statistics for monophasic cathodic vs biphasic stimulation of AN of cat. The data from their study is shown as the density kernel with mean of the data as the center of gravity. Corresponding model responses are shown with red squares.

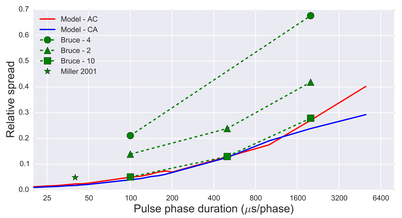

Fig.9 Bruce et al. 1999 reported increased RS with increasing the phase duration for biphasic pulses. Their data from 3 neurons along with data from Miller et al. 2001 is shown along with corresponding model predictions. Model predicts difference in RS between anodic-cathodic and cathodic-anodic pulses, but only at pulse durations beyond 1000 μs.

Discussion

- In this model, the strict threshold voltage criterion has been replaced by a more realistic smooth spike initiation zone, during which inhibitory input can cancel the spike initiation.
- Model fails to predict reduction in spike jitter with increasing level as reporter by Miller et al. 1999.
- Model predicts shorter latencies for biphasic stimulation than observed.
- Model over estimates the interaction between pulse phase duration and inter phase gap compared to data reported by Ramekers et al. 2014. However, the differences may be due to species specific (guinea pig in their study).
- This study shows that a model parametrized based on very few data points for monophasic stimulation can qualitatively predict the the responses to biphasic pulses of various shapes. Data fit to larger datasets for monophasic stimulation may improve the predicitve power of the model significantly.
- It may be possible to fit the model to individual human CI listeners using response statistics derived from eCAP recordings.

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