Large-scale analysis of patterned epiretinal stimulation for prosthesis design

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Objective: Electrical stimulation and recording using multi-electrode arrays presents a unique opportunity to improve the function of epiretinal prostheses by developing spatial patterns of stimulation that optimize elicited activity. However, analysis of retinal ganglion cell (RGC) spiking responses is limited by the laborious spike-sorting process: separating recorded spikes from the electrical artifact produced by passing current. A new algorithm (Mena et al, submitted) automates spike sorting for single electrode stimulation, but it has not been tested with spatial patterns of stimulation. Here we validate the performance of the algorithm by comparing it to extensive manual analysis that took months to perform, and use it to assess the effectiveness of spatial stimulation patterns for enhancing selectivity.

Methods: RGCs in isolated primate retina were stimulated and recorded using a custom 512-electrode array (60μm pitch, 8-15μm diameter, hexagonal grid). Charge-balanced triphasic current pulses were delivered on 1-7 electrodes at a time. Two types of multi-electrode stimulation were considered: (1) *bipolar* stimulation in which a neighboring electrode provides the return for current passed through the stimulating electrode, and (2) *local return* stimulation in which the surrounding six electrodes provide a return. To spike sort in the presence of stimulus artifact, a structured Gaussian process was used, in conjunction with knowledge of the typical spatiotemporal properties of the artifact, to estimate the artifact at each amplitude and subtract it from the recording. Known electrical templates from RGCs on the array recorded without electrical stimulation were then matched to these subtracted signals to assign spikes to particular neurons. Validation was performed by comparing the stimulation threshold for each cell (current level required to elicit a spike with probability 0.5) with the value obtained by manual analysis.

Results: For bipolar stimulation, the algorithm produced thresholds essentially identical to manual analysis for all 41 cells analyzed in 6 retinas. For local return stimulation, the algorithm performed similarly for 21 cells analyzed in 3 retinas. Future results will include application to a much larger data set, to test the improvements in selectivity obtained with bipolar and local return stimulation.

Conclusions: Automated spike sorting for electrical stimulation of the retina using multi-electrode arrays enables high-throughput experimentation and analysis. This permits the assessment of spatially patterned stimulation for enhancing the selectivity of an epiretinal prosthesis.

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