Reducing electrically induced spatial spread on the retina: Parameter optimization for retinal prostheses

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Introduction

Vision restoration in patients with outer retinal degenerative diseases such as Retinitis Pigmentosa (RP) and age-related macular degeneration (AMD), where the photoreceptors degenerate but the remainder retinal cells are still functional, rely on stimulating these viable cells. Once such approach are retinal prostheses which electrically stimulate the remaining cells and can be categorized according to the transplantation. Retinal protheses are typically composed of a camera, a processor, and an electrode array transplanted in either the sub, epi, or suprachoroidal space.

Despite the great promise they offer and the advancements in the field, the obtained visual acuity is low, due to poor spatial resolution of the induced activation. One reason is the induced activity spreads throughout the retina. Our goal here is to optimize the electrical pulse parameters, using current steering to confine the induced activity spread and thus enhance the spatial resolution.

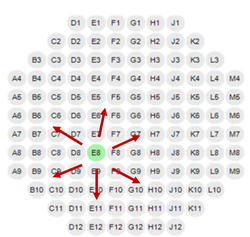
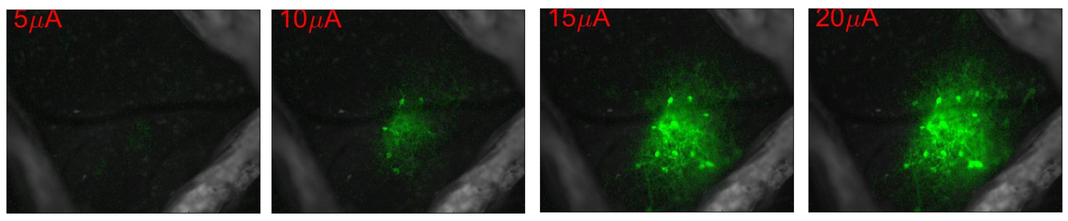


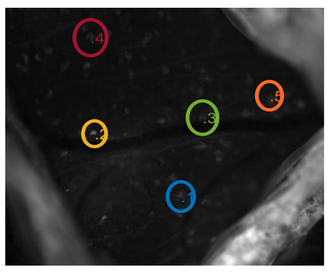
Image processing & Results

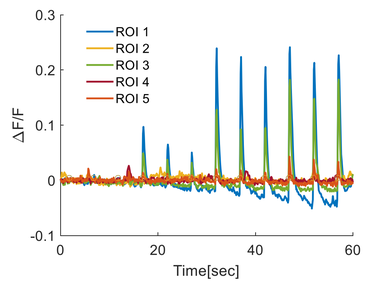
Spatial spread of the activated region was investigated by first finding the activation threshold by gradually increasing the current amplitude.



Representative acquired frames for increase currents with overlaid fluorescence change, highlighting the activation thresholds and the increasing spatial with increasing current amplitude

The induced fluorescence change was then calculated for each time point.

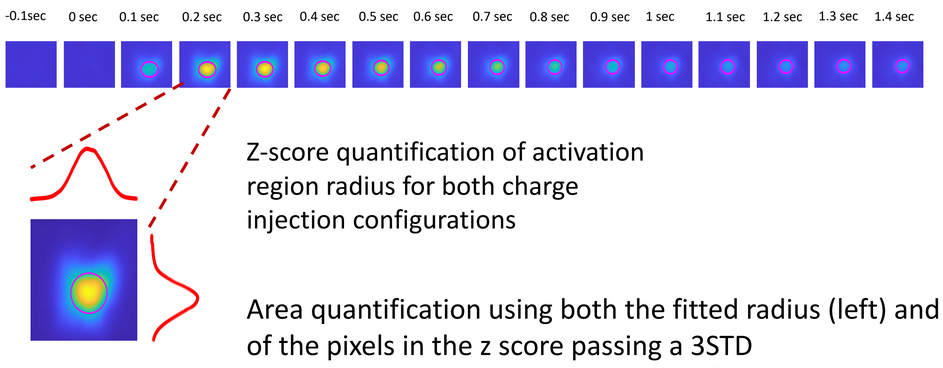




A FOV of the retina with several marked cells , with corresponding induced calcium change, revealing the 10μA activation threshold for this pulse duration

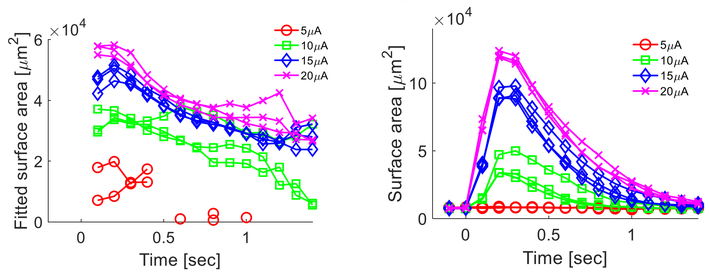
Activated region radius quantification

Next, to estimate the spatial spread, we calculated the z-scores through time for the fluorescence level of each pixel and fitted the activated region (using threshold of 3 standard deviations above the baseline) to a 2D Gaussian curve.



Z-score quantification of activation region radius for both charge injection configurations

Area quantification using both the fitted radius (left) and the surface area of the pixels in the z score passing a 3STD

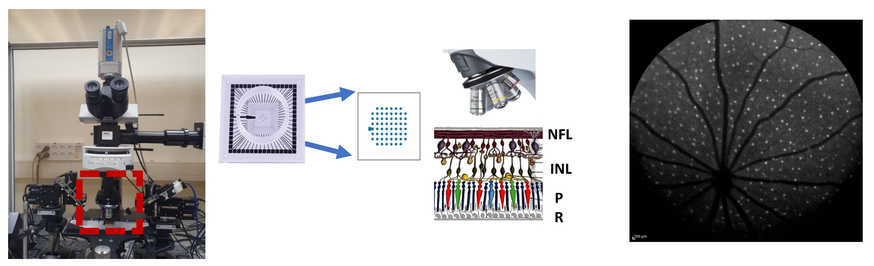


Conclusion

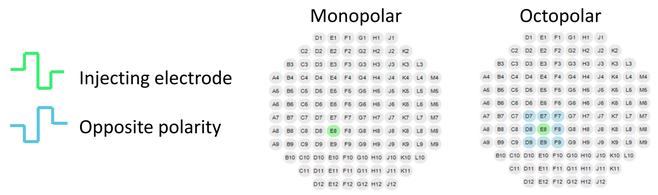
We investigated the effect of pulse and electrode configuration on the spatial spread of the induced RCG activity. We found that biphasic pulses induce a more spatially confined activity area compared to monophasic anodic pulses, and that using the surrounding electrodes to inject an opposite polarity current can further confine the induced spatial spread. Our next goal is to conduct experiments using the same pulse and electrode configurations in the blind animal model previously established by our group.

Methods

We used a transgenic breed of rats which express the genetically encoded calcium indicator under the thy 1 promoter enabling the optical visualization of retinal ganglion cells (RCG) activity. To investigate pulse and electrode configuration optimization in a subretinal stimulation setting, we isolated the retina and mounted it onto a multi electrode array. Fluorescence was visualized using a 10x objective.



Electrical pulses of various durations (100-1000μsec), current intensities (1-65 μA), configurations (anodic monophasic and anodic first biphasic) and electrode configurations (monopolar and octopolar) were delivered through the MEA.



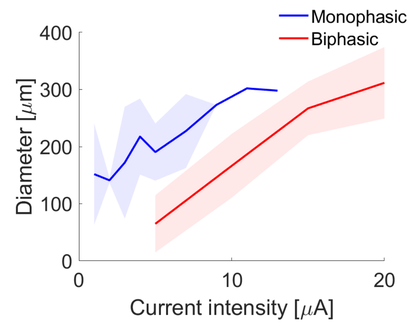
Results: configurations comparison

Pulse configuration effect

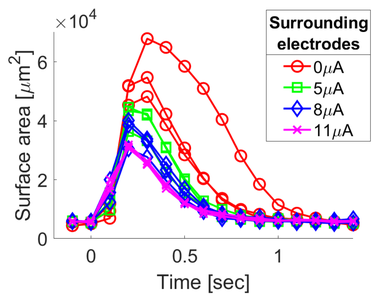
We compared the activity spread diameter for both pulse configurations:

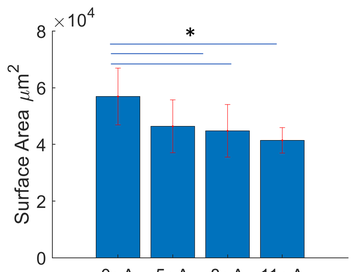
Monophasic (anodic) pulse:

Biphasic (anodic first) pulse:



Electrode configuration effect



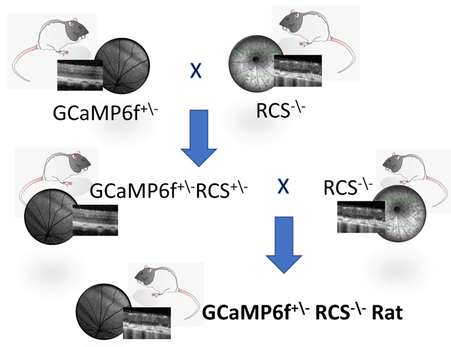


Opposite polarity current injected in the surrounding electrodes with increasing amplitudes resulted in confinement of the spatial spread.

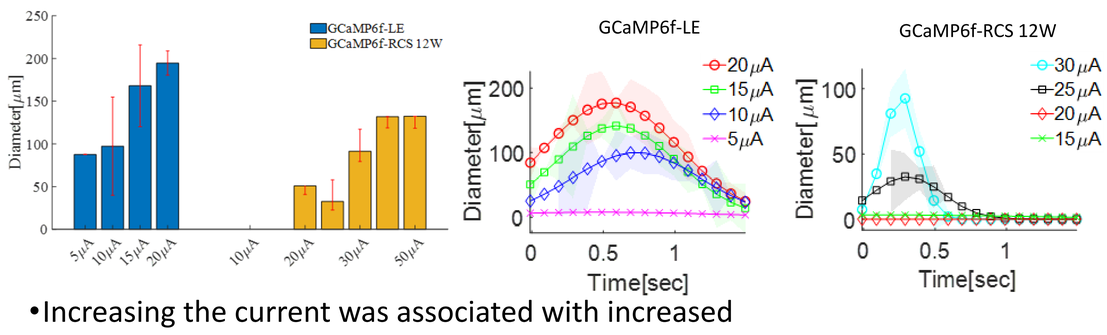
Surface area dynamics (left) and peak spread(right) in the octopolar configuration with increasing currents

Activity spread optimization in a blind animal model

We developed a novel blind rat model expressing the genetic calcium indicator GCaMP6f, under the promotor of Thy-1. This model allows us to investigate the effect of the same pulse parameters on the spatial spread of the RCG activity in blind rats.



Spatial spread of the activation area in GCaMP6f-RCS rat retina



- Increasing the current was associated with increased activation area diameter
- The activation area diameter decreased in the degenerative animal, compared to the WT

Azrad Leibovitch, Tamar, et anovell. "A GCaMP6f-RCS rat model for studying electrical stimulation in the degenerated retina." *Frontiers in Cell and Developmental Biology* 12 (2024): 1386141.