

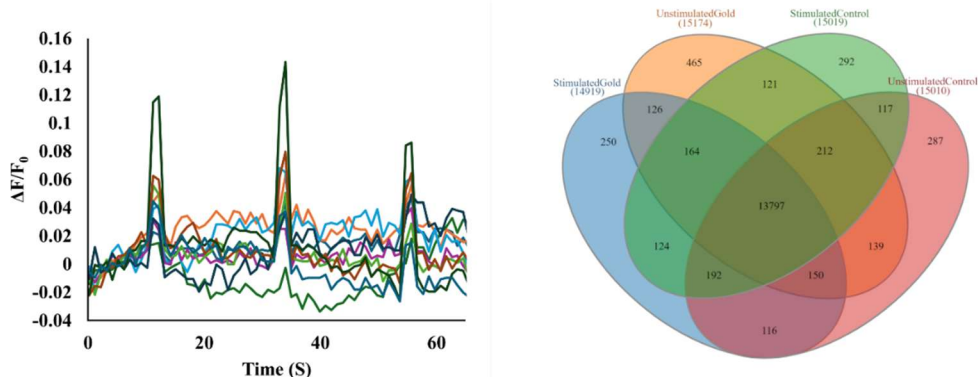
Response Properties of Retinal Neurons to Prosthetic Thermal Microarrays

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Loss of human neural retina leads to permanent vision loss due to mammalian retina lacking the ability to regenerate. A bioengineering approach to restore vision is with implantable retinal stimulation devices. Following ocular disease or trauma-induced loss of photoreceptors, retinal prosthetics can be implanted to stimulate remaining bipolar and retinal tissue to drive visual signaling. Gold-nanorod (GNR) coated polydimethylsiloxane (PDMS) microarrays can be used to thermally stimulate individual retinal cells with a high level of resolution and stability. These thermal microarrays are optimally designed to be stimulated via an extraocular near-infrared light source, requiring no additional wiring. The relationship between thermal warming and neuron calcium responses remains to be fully elucidated and will be analyzed in this work. We first analyzed calcium dynamics in retinal progenitor cells (RPCs) receiving thermal stimulation from GNR-PDMS microarrays to quantify response amplitudes and time courses relative to thermal stimulation paradigms. Next to identify differential expression of (RPCs) exposed to thermal stimulation, RNA-sequencing was performed comparing IR stimulated GNR-PDMS, IR-Stimulated PDMS, Non-stimulated GNR-PDMS, and Non-stimulated PDMS. Following RNA-seq analysis, a selection of genes with predicted association to thermal response were validated using qPCR validation and included *Cxcl10*, *Pde5a*, *Pdgfra*, *Cyclin* with controls *Gapdh*, and β -actin. Together, these calcium imaging and gene expression data provide a foundation for refining GNR-PDMS stimulation parameters, defining molecular mechanisms associated with neural thermal responses and evaluating the arrays as a potential retinal prosthesis.



Left: Normalized Fura-2 fluorescence amplitude ($\Delta F/F_0$) over time in individual retinal progenitor cells during 720 mW infrared stimulation of GNR-PDMS microarrays. The traces show variation in response amplitude among cells. **Right:** Venn diagram showing the overlap of protein-coding genes detected by initial RNA sequencing in stimulated GNR-PDMS, unstimulated GNR-PDMS, stimulated PDMS, and unstimulated PDMS conditions. Numbers indicate genes detected in each distinct region; 13,797 were detected in all four conditions.