Methods: Under anesthesia, the retina from rabbits was isolated and perfused in Ames Ringer. Large ganglion cells were selected for whole-cell recording using dim red or IR Nomarski illumination. A small hole was made in the inner limiting membrane to allow pipette access. The frequency vs. current firing properties of the ganglion cell were studied using 100pA current steps. Next, a thin insulated 100µm diameter Pt stimulus electrode was positioned at a 30 degree angle near the axon hillock/soma approximately 50µm above the retina. A series of 0.5msec ascending cathodic, followed by anodic current pulses (20msec apart) were used to examine how firing threshold varied laterally with soma proximity in 100µm steps. After recording, the morphology of the dye-filled ganglion cell was imaged and processed with anti-lucifer yellow antibodies for confocal microscopic reconstruction. The morphology of selected cells were entered into Neurolucida for segmentation, fitted with ion channels in NEURON, and imported into a novel electromagnetic-neuronal dynamics modeling program to simulate extracellular stimulation.
Results: When current steps were injected into the alpha cell body, a large pipette current was needed to elicit action potential threshold averaging 500±170pA (n=5 cells; mean ± std. dev). Some spike adaptation to firing was observed. Using epiretinal stimulus electrodes, action potentials were only generated by cathodic current pulses. When the electrode was placed adjacent to the cell body at the axon hillock region, thresholds for activation averaged 10.8±11.3nC (n= 5 cells; mean ± std. dev.). The spatial threshold for extracellular stimulation of the ganglion cells by the Pt electrode was localized to a region ~100µm around the initial segment/axon hillock of the cell body.
Conclusions: Large thinly insulated epiretinal stimulus electrodes activate action potentials in alpha ganglion cells in a spatially localized manner near the initial segment/soma region of the retinal ganglion cell. Synaptic activity may alter spike threshold.
Commercial Relationships: Ethan D. Cohen, None; **Esra Neufeld**; **Hazael Montanaro**, None; **Maria I. Iacono**, None; **Leonardo M. Angelone**, None; **Wolfgang Kainz**, None

Program Number: 3717 **Poster Board Number:** D0178
Presentation Time: 11:00 AM–12:45 PM
Electric stimulus duration alters network-mediated responses depending on retinal ganglion cell type
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Purpose: Despite some recent progress with retinal prosthetics the optimal duration for the electric stimulus remains unknown. Recently, we reported that an identical electric pulse elicits distinct responses in ON and OFF types of retinal ganglion cells (RGCs). The temporal properties to repetitive stimuli were also different in the two types. Thus, we hypothesize that varying the duration of the stimulus would alter the responses in different ways across different types of RGCs, thus raising a possibility to selectively activate one type over the other. Here, we systematically investigated network-mediated responses in various types of RGCs as a function of stimulus duration.
Methods: Cell-attached patch clamp was used to record spikes from RGCs in the rabbit retina explant. RGCs were classified as ON or OFF cells by their response to stationary flashes and further classified as Brisk Transient (BT) or Brisk Sustained (BS) subtypes by their electric responses. After cell type classification, monophasic half-sinusoidal stimuli with durations of 5-100ms and amplitudes adjusted to keep total charge constant were presented to targeted RGCs. Each stimulus was repeated 7 times. We recorded the spiking activity in 7 ON BT, 10 ON BS, 8 OFF BT, and 14 OFF BS cells.
Results: The pattern of network-mediated responses was unique for each type of RGC across a wide range of stimulus durations. We found that: 1) In ON cells, there was a distinct difference between BT and BS subtypes in number of spikes elicited by same stimulus duration but the distinction was less clear across OFF subtypes. 2) Across the durations tested, both types of ON cells showed dramatic changes in the number of evoked spikes while OFF cells showed smaller changes in their responses. 3) This disparity between ON and OFF cells resulted in the ratio of spikes elicited by the two types to be maximized at a stimulus duration of ~10 ms.
Conclusions: ON and OFF types of RGCs exhibited fundamental differences in responses to a wide range of durations of the electric stimulus, resulting in variable levels of ON vs. OFF selectivity at different durations. Together with our previous report that an electric stimulus evokes more physiological responses from ON cells than OFF cells, the finding here of a stimulus duration that maximizes the ON/OFF response ratio may offer enhanced clinical guidelines to retinal prosthetic community.
Commercial Relationships: Maesoon Im; **Shelley I. Fried**, None
Support: Boston VA Healthcare System (1I01RX000350-01A1) and NIH (R01EY023651)

Program Number: 3718 **Poster Board Number:** D0179
Presentation Time: 11:00 AM–12:45 PM
Relative power consumption at the electrode-retina interface during retinal stimulation with voltage versus current controlled stimulus pulses
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Purpose: The purpose of this study is to compare power consumed at the electrode-retina interface between rectangular current controlled and voltage controlled stimulus pulses.
Methods: Eleven Long Evans female rats under anesthesia were used for this in-vivo study. A 75 um diameter cylindrical Pt-Ir electrode was inserted into the left eye, and placed 50-100 um from the retina. Charge balanced biphasic voltage-controlled and current-controlled stimulus pulses of varying pulse width and amplitude were delivered to the retina. The pulse widths were 0.3 ms, 0.5 ms, 1 ms, and 2 ms. For each pulse width, voltage and current-controlled pulse trains with charge levels from 10 nC to 60 nC were delivered to the retina. An oscilloscope was used to measure and record the voltage waveform of the stimulus pulses at the electrode-retina interface. A sense resistor in the stimulus current path was used to measure and record the current waveform delivered to the retina. As previously reported, electrically evoked responses (EERs) were recorded from the superior colliculus (SC) in response to the retinal stimulation.
Results: The voltage and current waveforms delivered to the retina were used to measure the power consumed at the electrode-retina interface during the cathodic phase for each stimulus condition. For stimulus pulse widths of 0.3 ms, 0.5 ms, and 1 ms, there was no statistically significant difference between the power consumed by the voltage-controlled pulses versus the current-controlled pulses (student t-test, $p > 0.05$) at all charge levels tested. For stimulus pulse width of 2 ms, there was no statistically significant difference in the power consumed for stimulus charge levels of 20 nC and 30 nC (student t-test, $p > 0.05$), while voltage pulses consumed significantly more power than current pulses for charge levels of 40 nC and 50 nC (student t-test, $p < 0.05$).

Conclusions: In general, there is no significant difference in the power consumed at the electrode-retina interface between voltage and current controlled stimulus pulses, except for long pulse widths like 2ms and charge levels higher than 40 nC. This needs to be taken into consideration in combination with our previously reported results comparing the EERs in response to voltage versus current stimulus pulses when determining the most efficient stimulus parameters for electronic retinal prostheses.
Commercial Relationships: Kiran Nimmagadda; **Navya Davuluri**, None; **James D. Weiland**, None
Support: NSF CBET-1343193 and Research to Prevent Blindness

Program Number: 3719 **Poster Board Number:** D0180
Presentation Time: 11:00 AM–12:45 PM
Surgical feasibility of wide-field dual-array suprachoroidal–transretinal stimulation (STS) prosthesis in middle-sized animals
Takeshi Morimoto[2], Hiroyuki Kanda[2], Tomomitsu Miyoshi[3], Takao Endo[1], Tibor K. Lohmann[4, 2], Kohji Nishida[1], Takashi Fujikado[2]. [1]Ophthalmology, Osaka Univ Graduate Sch of Med, Suita, Japan; [2]Applied Visual Science, Osaka University Graduate School of Medicine, Suita, Japan; [3]Integrative Physiology, Osaka University Graduate School of Medicine, Suita, Japan; [4]Ophthatmology, Aachen RWTH Aachen University, Aachen, Germany.
Purpose: To investigate the feasibility of implanting a newly developed wide-field dual-array suprachoroidal–transretinal stimulation (STS) prosthesis in healthy dogs and cats.
Methods: Three healthy dogs and three healthy cats were used in this study. The STS dual array consisted of two arrays with 25 electrodes. The arrays were implanted into a scleral pocket of each of three healthy beagle dogs and three healthy cats under general anesthesia. Color fundus photography and Optical coherence tomography (OCT) were performed postoperatively. The animals were euthanized after the experimental period and the retinas were evaluated histologically.
Results: All the prostheses were successfully implanted without complications, and no serious complications occurred during the experimental period. The fixation of the implant was stable throughout the experimental period. Fundus photographs and OCT revealed no serious damage in the retina and choroid around the arrays.
Histologic evaluations showed good preservation of the retina over the electrode array.
Conclusions: Implantation of a newly developed wide-field dual-array STS retinal prosthesis into a scleral pocket of animals is surgically feasible and can be performed without significant damage to the retina or the animal. These findings indicate that it might be possible to implant more STS electrode arrays to cover a larger area of the retina to activate a larger visual field.
Commercial Relationships: Takeshi Morimoto, None; **Hiroyuki Kanda**, None; **Tomomitsu Miyoshi**; **Takao Endo**, None; **Tibor K. Lohmann**, None; **Kohji Nishida**, None; **Takashi Fujikado**, None

Program Number: 3720 **Poster Board Number:** D0181
Presentation Time: 11:00 AM–12:45 PM
Evaluation of the spatial resolution of electrode arrays for suprachoroidal retinal prosthesis by recording single-unit activities in the lateral geniculate nucleus
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Purpose: To evaluate the spatial resolution of an electrode array for retinal prosthesis by suprachoroidal–transretinal stimulation (STS), we recorded the single-unit activities of relay cells in the lateral geniculate nucleus (LGN).
Methods: Implantation surgeries were performed in cats (n = 4) under general anesthesia. The electrode array was chronically implanted into the scleral pocket of eyes. The electrode array had the same specifications as that used in the 2nd generation device of STS retinal prosthesis. This electrode array comprised 49 bullet-shaped electrodes that were 0.5 mm in diameter and 0.3 mm in height. The center-to-center distance of the electrodes was 0.75 mm. Under general anesthesia, acute experiments for the evaluation of spatial resolution of the electrode array were performed in 2–4 weeks after the implantation surgeries. The electrode position was identified by optical coherence tomography. Charge-balanced biphasic pulses were applied (pulse duration, 0.5 mm; current intensity, 0.1–1.0 mA) to the retina via each electrode independently. Stimulating trials were repeated 10 or 40 times, and response probabilities of single-unit activities in LGN relay neurons were analyzed. Their receptive fields were identified by visual stimulation, and the relationship between response probabilities and distances from the center of the receptive fields to the stimulating sites were evaluated.
Results: The response probabilities decreased as the distance between the stimulating site and center of its receptive field increased. With 0.5 mA of stimulus intensity, the responsive area exhibiting a response probability of more than 50% was identified within a range of 1 mm from the stimulating site.
Conclusions: These findings demonstrate that this electrode array is able to achieve localized stimulation. Moreover, spatial resolution by the STS approach appears to be acceptable, although the distance between the electrode and retina in this approach is larger than that in epi- or sub-retinal approaches.
Commercial Relationships: Hiroyuki Kanda, NIDEK (P); **Tomomitsu Miyoshi**, None; **Takeshi Morimoto**, None; **Takashi Fujikado**, NIDEK (P)
Support: coordination, support and training program for transnational research, MEXT, Japan

Program Number: 3721 **Poster Board Number:** D0182
Presentation Time: 11:00 AM–12:45 PM
Spatio-temporal characteristics of retinal responses to subretinal photovoltaic stimulation
Richard Smith[1], Elton Ho[2], Georges A. Goetz[2, 3], Xin Lei[3], Theodore Kamins[3], Jim Harris[3], Keith Mathieson[4], Daniel V. Palanker[2, 5], Alexander Sher[1]. [1]Santa Cruz Institute for Particle Physics, UC Santa Cruz, Santa Cruz, CA; [2]Hansen Experimental Physics Lab, Stanford, Palo Alto, CA; [3]Electrical Engineering, Stanford, Palo Alto, CA; [4]Institute of Photonics, University of Strathclyde, Glasgow, United Kingdom; [5]Ophthalmology, Stanford, Palo Alto, CA.
Purpose: To measure the spatio-temporal receptive fields of the retinal ganglion cells activated via subretinal photovoltaic prostheses in degenerate and wild-type rat retinas, and compare them to the natural light responses in healthy retinas.
Methods: Activity of the RGCs was measured in-vitro with a 512 channel multielectrode array. Photovoltaic array with 70μm pixels was placed on the photoreceptor side of healthy and degenerate (RCS) rat retinas. Prosthetic stimulation was performed with 880nm light pulsed at 20Hz and modulated by an LCD displaying binary white noise movies at frame rates of 10Hz and 20Hz. For stimulation of the healthy retina, the same LCD was used to display white noise movies at 30Hz frame rate with continuous visible light illumination. Spatio-temporal receptive fields of the RGCs were measured by