Mini-Symposia Title:

Artificial vision: latest progress in retinal prosthetics

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Theme:

- ○ 01. Biomedical Signal Processing
- ○ 02. Biomedical Imaging and Image Processing
- ○ 03. Micro/ Nano-bioengineering; Cellular/ Tissue Engineering &
- ○ 04. Computational Systems & Synthetic Biology; Multiscale modeling
- ○ 05. Cardiovascular and Respiratory Systems Engineering
- ◉ 06. Neural and Rehabilitation Engineering
- ○ 07. Biomedical Sensors and Wearable Systems
- ○ 08. Biorobotics and Biomechanics
- ○ 09. Therapeutic & Diagnostic Systems and Technologies
- ○ 10. Biomedical & Health Informatics
- ○ 11. Biomedical Engineering Education and Society
- ○ 12. Translational Engineering for Healthcare Innovation and Commercialization

Mini-Symposia Synopsis— Max 2000 Characters

Within roughly the past decade, the field of artificial vision has given at least some sight to people previously sightless. The first generation of the bionic retinas - microchips that replace failed retinal cells by collecting or amplifying light - is bringing a low-resolution version of sight to people, with Retinitis Pigmentosa and Aged-related Macular Degeneration, who for years saw nothing. Though significant progress has been made, challenges such as high-resolution version of light and wide-field stimulation still remains. This session will reveal the latest advances in this field including a new clinical device, an optogenetic approach, a new grading system to evaluate retinal health, a novel transparent 3D electrodes, and several insightful in-vitro studies. The future direction and potential challenges for the field will also be discussed.

Histology of chronically implanted suprachoroidal implants: An objective grading system centered on retinal health evaluation.

Samuel C. Eggenberger, The University of Sydney, Australia

Abstract— **Vision restoration to the blind using implantable electronics in the form of a retinal neurostimulator relies heavily on the viability of the host's neuronal network. Neurons – specifically retinal ganglion cells (RGCs) - must be able to fire as a result of electrical stimulation and to transmit signals from the eye to the brain for interpretation. Chronic implantation in animal models, followed by histological analysis of the retina is typically used to evaluate the local effects of the prosthesis. A grading system is presented, which is centered around the morphology of retinal layers.**

I. INTRODUCTION

Electrical stimulation of the retina from the suprachoroidal space to restore functional vision in people who have lost it due to retinal degeneration has previously been demonstrated in humans [1]. Comparatively easy surgical access to the proximity of the retina characterizes this approach. Physical separation between the target neurons and the electrodes through the choroid may also improve long-term performance of suprachoroidal devices compared to their epiretinal or subretinal counterparts [2].

The implantation procedure, as well as the long-term presence of a device in the eye, have the potential to disrupt the natural anatomy and function of the tissue. In order to characterize the chronic effects of a suprachoroidal prosthesis in an animal model, a grading system is proposed, which considers the role each retinal layer plays during electrical stimulation.

II. METHODS

An analysis of the literature on retinal prostheses was performed to characterize the importance of the different layers of the mammalian retina during electrical stimulation and their role in transmission of the stimulated signal to the brain. Non-degenerate retinal anatomy was used to define the grading system, as sighted animals are often used during pre-clinical trials.

III. RESULTS

The retinal pigmented epithelium (RPE), outer nuclear layer and outer plexiform layers are typically rendered dysfunctional by degenerative disorders such as retinitis pigmentosa or age-related macular degeneration. They were therefore identified as having the least impact on the ability of the neural retina to be stimulated electrically to restore vision. The inner nuclear layer and inner plexiform layer, due to their possible recruitment by suprachoroidal stimulation, could impact the excitability of the retina, should their health be compromised by the presence of a prosthesis. Finally, the loss of RGCs and their axons in the nerve fiber layer would substantially impede the ability of a device to elicit visual percepts. Local host responses such as fibrosis may influence the charge required to trigger a neural response, but this effect is difficult to measure. Therefore, a two-part grading system was defined, in order to separate the local host response around the implant from the effects, associated or otherwise with the device, on the neural tissue.

The retinal health scale focuses on the depth of the involvement of the retinal tissue, and on the absence or presence of retinal hemorrhage and detachment. The retinal condition is rated on a scale from 'none', meaning that no retinal involvement is visible, to 'severe', where retinal degeneration with significant retinal ganglion cell loss is observed. 'Mild' characterizes damage which extends to the outer retinal layers and 'moderate' characterizes involvement of the inner retinal layers without significant ganglionic layer loss.

The second scale is experiment-subjective and can be used to establish a hierarchy of host response levels within sample groups or sub-groups. Fibrosis, histiocytic response and 'other damage' are rated from '0' to '3' meaning 'no response' to 'most severe response observed in the experimental group', respectively.

IV. DISCUSSION & CONCLUSION

The proposed grading system allows for the observed host response to be calibrated on the retinal health. For example, the most severe response observed in an experiment may only cause mild retinal damage, if any. It provides an objective scale to evaluate the effects of retinal prostheses on the neural tissue, therefore allowing better comparison between experimental units and studies.

ACKNOWLEDGMENT

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REFERENCES

[1] Ayton, L.N., et al., *First-in-Human Trial of a Novel Suprachoroidal Retinal Prosthesis.* PLOS ONE, 2014. **9**(12): p. e115239.

[2] Bareket, L., et al., *Progress in artificial vision through suprachoroidal retinal implants.* J Neural Eng, 2017. **14**(4): p. 045002.

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Injectable, wide-field, and photovoltaic epi-retinal prosthesis

Diego Ghezzi, École polytechnique fédérale de Lausanne

Abstract— **POLYRETINA is a retinal prosthesis designed to restore a large field of view in blind patients. All the steps performed by our research group to translate this research activity into a clinical device will be presented.**

I. INTRODUCTION

Blindness affects more than 39 million people worldwide that suffer either from the decrease of their visual acuity or from the constriction of their visual field. Visual prostheses are neuroprostheses able to restore artificial vision via electrical stimulation of the visual system. In particular, retinal prostheses showed the restoration of a coarse form of vision in patients affected by retinitis pigmentosa, such as single letters discrimination and simple objects recognition. Despite some progress in retinal prosthetics, several challenges remain open, such as the improvement of visual acuity and the enlargement of the visual field above the thresholds of blindness. An agreed-upon strategy to improve visual acuity is to increase the electrode density, while a large visual field could be attained by enlarging the retinal coverage with a larger prosthesis.

II. METHODS

To overcome this problem, we designed an injectable, wide-field, and photovoltaic epi-retinal prosthesis, called POLYRETINA [1]. To validate the device, we implemented several methods, including in-silico, in-vitro, ex-vivo, and in-vivo approaches.

III. RESULTS

POLYRETINA is based on organic electronic materials embedded into a stretchable substrate, and it is manufactured with microfabrication methods, adapted to soft, temperature-sensitive and solvent-sensitive materials (Fig. 1). It contains 10,498 photovoltaic electrodes (diameter of 80 µm and pitch of 120 µm) distributed with a pixel density of 80.33 pixels mm^{-2}. The pixels cover an active area of 12.9 mm in diameter; thus, the prosthesis covers a visual angle of 46.3 °.

The optoelectronic performances of POLYRETINA were validated in-vitro by using a kelvin probe force microscope and by recording the photovoltage and photocurrent generated by the photovoltaic pixels.

We performed accelerated ageing tests to estimate in-vitro the lifetime of the device, and we proved its safety using thermal modelling and by performing an assay for in-vitro cytotoxicity.

The stimulation efficiency of POLYRETINA was evaluated via a hybrid in-silico and ex-vivo approach. We recorded the evoked activity of retinas explanted from retinal degeneration 10 mice upon photovoltaic stimulation. POLYRETINA stimulation efficiently rescued indirect network-mediated activity in the retinal ganglion cells. Moreover, by pairing electrophysiological results with a biophysical model, we showed that POLYRETINA stimulation recruited the lateral inhibition network formed by Amacrine cells and focused the activation of retinal ganglion cells leading to a decrease in their network-mediated electrical receptive fields [2].

Preclinical experiments with Göttingen minipigs showed the injection and epi-retinal placement of the POLYRETINA device.

Figure 1. Picture of the POLYRETINA prosthesis.

IV. DISCUSSION & CONCLUSION

POLYRETINA is a promising retinal prosthesis to restore artificial vision in blind patients affected by retinitis pigmentosa.

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REFERENCES

[1] L. Ferlauto *et al.*, "Design and validation of a foldable and photovoltaic wide-field epiretinal prosthesis," *Nature Communications*, vol. 9, no. 1, p. 992, 2018.

[2] N. A. L. Chenais, M. J. I. A. Leccardi, and D. Ghezzi, "Capacitive-like photovoltaic epiretinal stimulation enhances and narrows the network-mediated activity of retinal ganglion cells by recruiting the lateral inhibitory network," *J. Neural Eng.*, vol. 16, no. 6, p. 066009, Oct. 2019.

Optogenetic Approach to Retinal Vision Restoration for AMD Patients

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***Abstract*— Optogenetic technique for vision restoration confers photosensitivity to surviving inner retinal cells. This approach offers a promising prosthetic perspective to a minimally invasive vision restoration to patients suffering from age-related macular degeneration. A see-through optoelectronic microsystem is proposed here to restore central vision.**

I. INTRODUCTION

Age-related macular degeneration (AMD) is one of the leading causes of severe vision loss in seniors. It is characterized by blurring, distortion or loss of central vision as the small central portion of the retina, called macula, degrades. AMD, specially the dry form, is often refractory to current medical treatments. Therefore, a visual prosthetic tool becomes a vital solution to restore vision. Optogenetic vision restoration, which involves photosensitizing retinal neurons, can offer a less complex and more efficient approach than conventional retinal prosthesis implant to restore functional vision [1].

II. METHODS

AMD disease is a progressive degeneration of cones photoreceptors in macula that results in loss of central vision. Optogenetic vision restoration to AMD patients currently involves several challenges. Almost all of recent researches on optogenetic retinal prosthesis addressed other retinal degeneration diseases such as Retinitis Pigmentosa (RP) and only mentioned AMD as their possible application [2]. Foveal vision restoration, eye movement, retinal cells' crosstalk and limited visual field are some of the most important challenges that have thoroughly reviewed in [1]. Our proposed optoelectronic headset for optogenetic vision restoration addresses these challenges (Fig. 1). The proposed approach only stimulates the inner retinal cells associated with degenerated area with relevant visual information and allows the patients to use their healthy photoreceptors.

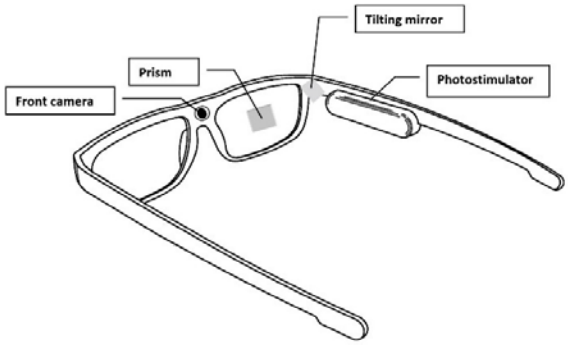

Figure 1. Projected glasses for optogenetic vision restoration

III. RESULTS

A see-through optoelectronic device on which all components can be mounted and meanwhile it allows the patients to normally use the part of their vision which is functional is proposed. An initial design of such a see-through optoelectronic headset is given in Fig. 1. The design has been validated through simulation tool ZEMAX using optical models of lenses and human eye. The validation ensures that the stimulation pattern is well-received at retina level (Fig. 2).

Figure 2. Image simulation result obtained by our optical model

IV. DISCUSSION & CONCLUSION

A see-through optoelectronic headset for optogenetic vision restoration to AMD patients has been proposed. The design has been validated by simulation of optical path. The next step will be to build the goggle and to validate it with eye model and bio-test.

ACKNOWLEDGMENT

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REFERENCES

[1] Montazerijouibari, L., et al., Optogenetic Stimulation for Restoring Vision to Patients Suffering from Retinal Degenerative Diseases: Current Strategies and Future Directions. IEEE Transactions on biomedical circuits and systems, In press, 2019.

[2] Nirenberg, S. and C. Pandarinath, *Retinal prosthetic strategy with the capacity to restore normal vision.* Proceedings of the National Academy of Sciences, 2012. 109(37): p. 15012-15017.

Depolarization in Membrane Potential of RGCs by High Frequency Electric Stimulation Underlies Different Non-monotonic Responses of ON and OFF RGCs

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Abstract— **High frequency electric stimulation of the retina has received increasing attention since it may allow preferential activation of ON vs. OFF cell types. Here, we investigated the underlying mechanism for the response differences between the two types. We found that high frequency stimulation depolarized the membrane potential of RGCs. The responses of RGCs became stronger with increasing depolarization, but above a certain point (referred to as the breakdown level), further increases impeded spiking. Breakdown levels were different for ON and OFF cells, resulting in their differential responses.**

I. INTRODUCTION

In a previous study [1], our group showed that retinal ganglion cells (RGCs) exhibit non-monotonic responses to high frequency electrical stimulation. We also found that ON and OFF RGCs show peak firing rates at different current amplitudes, suggesting the possibility of preferential activation of individual cell types. In this study, we investigated the mechanism underlying the different non-monotonic responses of ON and OFF RGCs to high frequency (2 kHz) stimulation.

II. METHODS

We obtained whole-cell current clamp recordings from alpha RGCs in the isolated retinas of wild-type mice (C57BJ/6J). Alpha RGCs were targeted using their large soma (>20 μm) and classified as ON or OFF types by their light responses. In particular, we focused on ON and OFF brisk-sustained cells whose light-evoked responses persisted > 500 ms without exhibiting transient peaks in their peristimulus time histogram. We recorded responses from 8 ON and 8 OFF RGCs. A biphasic sinusoidal electric stimulus (2 kHz, duration of 1 s, peak amplitude ranged from 10 μA to 100 μA) was extracellularly delivered to elicit responses in targeted cells.

III. RESULTS

We found that: 1) High frequency stimulation depolarized the membrane potential of the RGCs. The membrane potential of RGCs depolarized monotonically up to ~20 mV as the amplitude of stimulation increased. 2) We observed that an increasing level of membrane potential was associated with non-monotonic response curves of RGCs: initial increase and subsequent decrease in firing rate. Up to the breakdown level [2], firing rate increased linearly as a function of a membrane potential (R^2 = 0.881 and 0.728 for ON and OFF cells, respectively). However, further increase in the membrane potential over the breakdown level caused the RGCs to gradually shut down their responses, resulting in the prolonged inability to generate action potentials. RGCs also showed a weak correlation between firing rate and membrane potential after the breakdown (R^2 = 0.049 and 0.019 for ON and OFF cells, respectively). The ON and OFF cells showed breakdowns when they are depolarized by 15.72 ± 1.38 mV and 11.89 ± 2.08 mV, respectively. 3) The ON cells showed breakdown at lower current amplitudes than the OFF cells, resulting in the differential non-monotonic responses of ON and OFF RGCs. Peak firing rates of the ON and OFF cells were observed at current amplitudes of 48.57 ± 4.04 μA and 84.00 ± 4.00 μA ($p < 0.001$), respectively.

IV. DISCUSSION & CONCLUSION

We found that high frequency stimulation depolarized the membrane potential in RGCs. The response of the RGCs became stronger up to certain levels of stimulation (breakdown level), above which RGC activity began to decrease. The onsets of the breakdown in ON and OFF cells occurred at different stimulus amplitudes

REFERENCES

[1] P. Twyford, C. Cai, and S. I. Fried, "Differential responses to high-frequency electrical stimulation in ON and OFF retinal ganglion cells," *J. Neural Eng.,* vol. 11, 025011, Feb. 2014.

[2] T. Kameneva, M. I. Maturana, A. E. Hadjinicolaou, S. L. Cloherty, M. R. Ibbotson, D. B. Grayden, A. N. Burkitt, and H. Meffin, "Retinal ganglion cells: mechanisms underlying depolarization block and differential responses to high frequency electrical stimulation of ON and OFF cells," *J. Neural Eng.,* vol. 13, 016017, Jan. 2016.

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A comparison of responses to electrical stimulation: in vitro vs. human perception

James D. Weiland, University of Michigan

Abstract— **Electrical stimulation of the retina can provide perception of light to people otherwise blind from retinal degeneration. A significant number of studies have used an in vitro retina preparation to study the basic mechanisms of how retinal cells respond to electrical stimulation. Studies include threshold to stimulation, temporal aspects of stimulation, and shape of stimulus response area. Some of these measurements can be made in humans with implants, though to a lesser degree of accuracy.**

I. INTRODUCTION

Retinal prostheses can provide artificial vision to someone who has lost most ability to sense light naturally. Patients with implants use artificial vision to help with navigation and feeling socially connected. In controlled experiments, implant patients can discriminate between letters in a set and common objects.

II. METHODS

In vitro retina experiments are performed typically with mouse or rat retina, though some experiments are reported with amphibian or non-human primate retina [1]. The retina is dissected and kept viable in a bath with appropriate chemicals, oxygen, and kept at body temperature, for mammals. Electrical stimulation is delivered via either an electrode on a manipulator or a multi-electrode array (MEA) built into the dish or well used to hold the retina. A weighted screen holds the retina in place and allows access to retinal cells.

Human psychophysics experiments are conducted by varying stimulus parameters and users responding with a "yes" or "no" to indicate perception [2]. Users enter responses on a keyboard. Users will also draw the shape of perceptions on touch screens or report the orientation of lines, also known as grating acuity testing [3].

III. RESULTS

We will review in vitro vs. human percpetion results in three areas: threshold, persistence, and shape.

Threshold. In vitro thresholds are consisently lower than human perception threholds, but relative measures can be made. Stimulus setttings that reduce threshold in vitro have also shown to reduce perceptual threshold. For example, the use of interphase gap and a hyperpolarizing pre-pulse both reduce in vitro and perceptual thresholds [4].

Persistence. Human users report fading of perceptions. A train of pulses is perceived as decreasingly bright even if the stimulus amplitude stays the same. However, direct ganglion cell stimulation (non-synaptic) can follow stimulus pulses at rates well over 100 pulses per second, but network driven ganglion cell activity is inhibited at around 10 pulses/second. Inhibitory circuits in the retina may lead to reduction in excitability and the loss of perception in human studies.

Shape. The shape of stimulus area is difficult to quanitfy reliably in humans. Touch screens and arranging blocks into shapes can provide a means for the user to describe the perception shapes. Imaging approaches are used in vitro, such as calcium sensitive dyes [5]. One study showed convincingly that long pulses could create more focal percept in vitro, and supported that with a pilot clinical study, where the results were less clear. Modeling of retinal stimulation suggests that activation of axons of passage can result in elongated percepts, which was confirmed in both human and in vitro experiments.

IV. DISCUSSION & CONCLUSION

In vitro retina is a valuable tool for studying electrical stimulation of the retina. It is an efficient means for evaluating many aspects of retinal stimulation.

ACKNOWLEDGMENT

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REFERENCES

[1] Weiland JD, Walston ST, Humayun MS. Electrical stimulation of the retina to produce artificial vision. *Annual review of vision science.* 2016;2:273-294.

[2] de Balthasar C, Patel S, Roy A, Freda R, Greenwald S, Horsager A, Mahadevappa M, Yanai D, McMahon MJ, Humayun MS, Greenberg RJ, Weiland JD, Fine I. Factors affecting perceptual thresholds in epiretinal prostheses. *Invest Ophthalmol Vis Sci.* 2008;49(6):2303-2314.

[3] Beyeler M, Nanduri D, Weiland JD, Rokem A, Boynton GM, Fine I. A model of ganglion axon pathways accounts for percepts elicited by retinal implants. *Scientific Reports.* 2019;9(1):9199.

[4] Weitz AC, Behrend MR, Ahuja AK, Christopher P, Wei J, Wuyyuru V, Patel U, Greenberg RJ, Humayun MS, Chow RH, Weiland JD. Interphase gap as a means to reduce electrical stimulation thresholds for epiretinal prostheses. *J Neural Eng.* 2014;11(1):016007.

[5] Weitz AC, Nanduri D, Behrend MR, Gonzalez-Calle A, Greenberg RJ, Humayun MS, Chow RH, Weiland JD. Improving the spatial resolution of epiretinal implants by increasing stimulus pulse duration. *Sci Transl Med.* 2015;7(318):318ra203.

A subretinal prosthesis based on transparent 3D electrodes

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***Abstract*— We have developed a subretinal prosthesis based on a transparent 3D electrodes array and a photodiode/stimulation circuitry, tested them in *in-vitro* conditions and assembled into an integrated device. Various versions of integrated devices are under examination in *in-vitro* as well as *in-vivo* conditions.**

I. INTRODUCTION

Among different approaches toward retinal prostheses to restore the vision of the blinds, subretinal prostheses have advantages such as the robust fixation of the stimulating electrodes and the preserved natural physiological signal pathway, in which the final cells in the retina (retinal ganglion cells) receive information from bipolar cells. Also, subretinal prostheses can keep the minimum distance between the stimulating electrodes and the target cells (bipolar cells) so that they can be stimulated with the highest efficiency due to the minimum loss of current, although the surgery to implant a subretinal device is more challenging than other types of retinal implants.

We have developed a biocompatible subretinal prosthesis consisting of a 3D microelectrodes array, a pulse generating circuitry and photodiodes integrated circuit (IC), and a power and data receiving coil. Each technical component has been evaluated in either *in-vitro* or *in-vivo* environments, and integrated into a single assembly.

II. METHODS

The electrodes array was fabricated based on a flexible and transparent substrate, which allows for light to go through to get the photodiodes underneath the electrodes' substrate [1]. Polydimethylsiloxane (PDMS) with a thickness of 150 μm was used as a substrate of electrodes to realize the transparent electrodes array. We fabricated 98-channel electrodes with variable hexagonal arrangement of reference electrodes, for 64-pixel stimulation. The electrodes were coated with Pt, with a diameter of 150 μm, a height of 20 μm, and the pitch between the electrodes of 350 μm. The fabricated 3D electrodes array was further assembled with the IC to stimulate retinal cells subretinally in response to the incident light to the photodiodes.

Each of the electrodes array and the IC was tested in *in-vitro* environments using mouse retina. The developed electrodes delivered stimulation pulses to the retinal patch and the response of the retina was recorded by a commercial 64-channel multi-electrode array (MEA) system. In addition, the electrodes and the IC as an integrated device has been experimented in *in-vitro* condition using porcine retina.

III. RESULTS

Fig. 1 shows the transparent 3D electrodes array, the photodiodes and pulse generating IC, and the integrated assembly of them. For full implantation, the power and data could be received by a coil connected to the IC. From the *in-vitro* experiments, the developed 3D electrodes demonstrated the capability of subretinal stimulation with a lower threshold charge density than 2D retinal electrodes. Also, the developed IC showed that all channels worked properly on benchtop as well as in *in-vitro* setups.

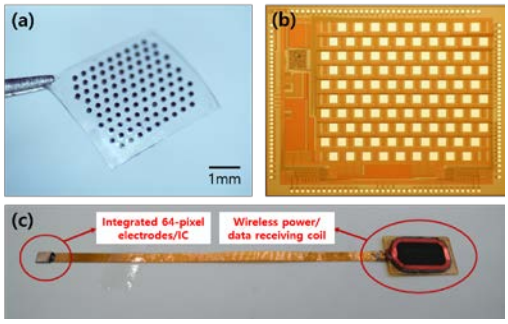

Figure 1. (a) Transparent 3D electrodes array and (b) photodiodes and pulse generating IC for 64-pixel stimulation, and (c) final integrated assembly including all components.

IV. DISCUSSION & CONCLUSION

In-vitro and *in-vivo* evaluation of the various versions of integrated devices is now underway, along with the refinement of each component such as the electrodes, the IC, and biocompatible packaging. The current 64-pixel system will be expanded to 256-pixel system or more in the near future.

REFERENCES

[1] H.W. Seo et al., "A 3D flexible microelectrode array for subretinal stimulation," *J. Neural Engineering*, Vol. 16, Art.-No. 056016, 2019.

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