CORA Cork Open Research Archive
Cartlann Taighde Oscailte Chorcaí

Title	Comparison between different optical systems for optogenetics based head mounted device for retina pigmentosa
Authors	Soltan, Ahmed;Liu, Yu;Armstrong, Niall;Akhter, Mahbub;Corbett, Brian;Degenaar, Patrick
Publication date	2019-10-07
Original Citation	Soltan, A., Liu, Y., Armstrong, N., Akhter, M., Corbett, B. and Degenaar, P. (2019) 'Comparison between different optical systems for optogenetics based head mounted device for retina pigmentosa', 2019 41st Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), Berlin, Germany, 23-27 July, pp. 3820385. doi: 10.1109/EMBC.2019.8857545
Type of publication	Conference item
Link to publisher's version	https://ieeexplore.ieee.org/document/8857545 - 10.1109/EMBC.2019.8857545https://embc.embs.org/2019/
Rights	© 2019, IEEE. Personal use of this material is permitted. Permission from IEEE must be obtained for all other uses, in any current or future media, including reprinting/republishing this material for advertising or promotional purposes, creating new collective works, for resale or redistribution to servers or lists, or reuse of any copyrighted component of this work in other works.
Download date	2024-03-28 14:34:31
Item downloaded from	https://hdl.handle.net/10468/9637

UCC
University College Cork, Ireland
Coláiste na hOllscoile Corcaigh

Comparison between different optical systems for optogenetics based head mounted device for Retina Pigmentosa

Ahmed Soltan[1], Niall Armstrong[2], Mahbub Akhter[3], Brian Corbett[3], Patrick Degenaar[1]
[1.] School of Engineering, Newcastle University, Newcastle upon Tyne, NE1 7RU, UK
[2.] C4 Sightcare Ltd, Northumberland House, Newcastle upon Tyne, NE1 8ER, UK
[3.] Tyndall National Institute, Cork T12R5CP, Ireland
Email:{ahmed.abd-el-aal, patrick.degenaar}@newcastle.ac.uk

***Abstract*— Optogenetics is a fast growing neuromodulation techniques as it can remotely stimulate neural activities of a genetically modified cells. The advantage of remotely controlling the neural activity triggered researchers to implement a headset to externally stimulate retina cells for people with retina pigmentosa. The wearable device will require an efficient optical system to focus the transmitted light pattern into the retina surface. In this work, three different lenses; contact lens, folded prism and linear lenses are used to evaluate the impact of the lens on the headset performance. A 90x90 µLED display is used as a light source and the optical efficiency for each lens is measured for different points over the lens area. Moreover, the impact of each lens on the headset performance in power and processing will be discussed in this work.**

Keywords:- Optogenetics, micro-display, wearable device, headset, linear lens, folded prism, contact lens.

I. INTRODUCTION

Recently, optogenetics have gained a great attention in research due its advantages of selectivity and the ability to do simultaneously both recording and stimulations with small artefacts [1, 2]. Moreover, optogenetics can be used for both stimulation and inhibition using different colors based on the type of genes used [3]. Another vital advantage of optogenetics is that it does not need direct contact to the targeted cell for stimulation. However, this raises a limitation on the light source as the light power has to be enough to achieve the required penetration [4]. Hence, a lot of effort has been done to propose implantable optrodes for optogenetics based neural modulation [5, 6, 7, 8]. Moreover, high density microdisplays have been developed in order to achieve high-density stimulation points [9, 10, 11].

According to the World Health Organization (WHO) in 2014, there are 39 million blind people worldwide [12]. Although some of blindness causes can be treated by drugs or surgical operations, there are some cases which requires implanted devices for curing. Some implantable target the retina for stimulations in case of having the optical nerve is functional such as Retinitis Pigmentosa. On the other hand, some cases requires stimulation at the level of visual cortex when the optical nerve is not functional [12]. Yet, all the previously proposed techniques are invasive approach [13]. However, optogenetics based stimulation is able to stimulate the neurons without the need for direct contact to the tissue.

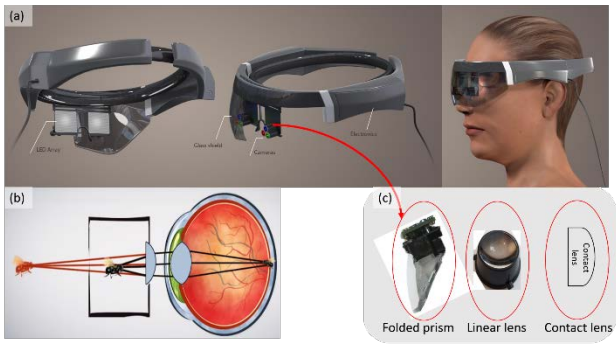


Fig. 1 (a) conceptual diagram show the proposed headset and the location of the lenses in the headset, (b) simple diagram to illustrates the concept of delivering the image from infinity to the retina surface, (c) the three different lenses used in the headset to evaluate the headset performance.

Hence, retina cells can be stimulated externally without the need for invasive devices. This is achievable if the wearable device is able to deliver light intensity above the stimulation threshold which is 0.7mW/mm^2 for Channelrhodopsin-2 [1]. Channelrhodopsin-2 is the gene integrated with retina cells in order to make it sensitive to the blue light (λ =470nm) for stimulation [3] .

In [14], a headset for stimulating retina cells externally is proposed and proved that is can deliver enough light for stimulation at the retina surface. This work discuss the optical system and its performance for the headset presented in [14]. A conceptual diagram for the headset is depicted in Fig. 1 (a) which shows the different components of the device including the lenses. The headset performance is evaluated using three different lenses; contact lens, folded prism and linear lens as shown in Fig. 1 (c) [15, 16]. The purpose of the lens in the headset is to focus the light into the retina surface. Moreover, the optical system will deliver the pattern from the microdisplay to the retina as if the microdisplay at infinity as depicted in Fig. 1 (b). Moreover, the impact of the different lenses on the image resolution and the power consumption will be discussed in this work.

II. DIFFERENT LENS

In this work, three different lenses are used to build three different optical system for the headset. The aim of the optical system is to focus the image on the retina surface and maximizing the amount of light delivery to the retina surface.

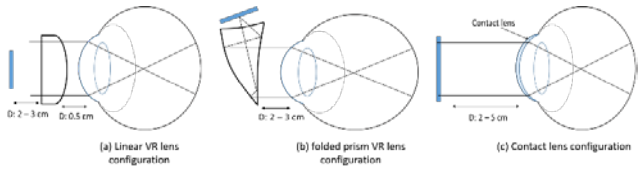


Fig. 2 (a) the optical system arrangement with the linear VR lens from oculus (b) the configuration with the folded prism VR lens which shows the compactness of the headset, (c) rift the optical configuration in case of using contact lens which shows the microdisplay at a distance of 2-5cm from the eye,

The three used lenses are contact lens, folded prism virtual reality (VR) lens and linear VR lens. Brief description for each lens its impact on the headset is given in the following subsections.

A. *Linear VR lens*

In this configuration, a linear VR lens from oculus rift is used to build the optical system as depicted in Fig. 2 (a). In this arrangement, the cell is placed very close to the eye (at 0.5cm) while the microdisplay is placed at a distance of 2-3 cm from the lens. This makes the headset very bulky compared to the other two configurations. Due to the linear structure of the lens, the image distortion is less than the distortion due to the folded prism lens.

B. *Folded prism VR*

In this work, the folded prism VR lens from an eMagin z800 VR headset to build the optical system of the headset. The optics configuration in this case is illustrated in Fig. 2 (b). The VR lens is designed to have the microdisplay as the image source and the human retina as the image plan. The microdisplay is located at the bottom on the lens as shown in Fig. 2 (b). In order to have the VR system compact and light, it is designed to have to two optical paths. The first optical path is formed by a wedge – shaped freeform surface (FFS) prism which is built from multiple individual surfaces. The second optical path of the VR system consists of the cemented auxiliary lens. In this configuration, the lens is placed in a distance of 2 -3 cm from the pupil.

C. *Contact lens*

The optics arrangement in the case of contact lens is depicted in Fig. 2 (c). The µLED matrix (the light source) is placed at a distance of 2 -5cm from the patient's eye. This spacing is similar to distance for normal glasses. On the other hand, the contact lens is placed on the patient's eye. Hence, this decreases the size and weight of the headset compared to the other types of the lenses.

The main problem for this arrangement, is the contact lens size. In order to achieve the required focus from the contact lens, a custom one of D-factor 52 is fabricated. Hence, the lens is heavy to be stable on the pupil.

III. RESULTS

A test platform is built to evaluate the performance of the three lenses as shown in Fig. 3. The platform is designed to be flexible to move in the three dimensional XYZ.

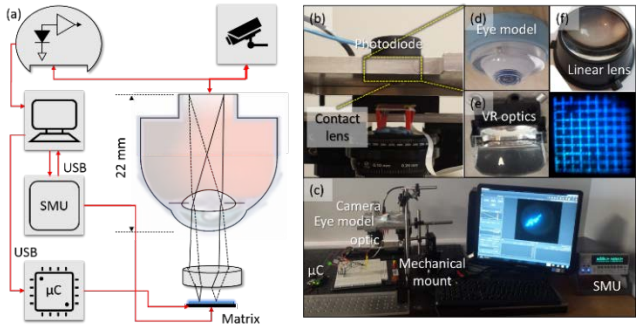


Fig. 3 (a) the test platform for the three lenses which shows the microdisplay and the photodiode for light measurement (b) the photodiode used for measuring the light intensity, (c) image of the setup used for the measurement (d) image of the eye model used to emulate the eye impact on the light signal, (e) an image of the folded prism lens, (f) photo of the linear lens and an exemplar pattern that captured at the backside of the eye model after the optics and the eye model.

This to enable the accurate alignment of the eye model, the optical system and the microdisplay. Also, this degree of freedom of the movement enabled fine tuning of the distance between the three components of the system. An eye model from Ocular instrument (OEMI-7) is used to simulate the impact of the eye on the image. The model is filled with a liquid from same company. An image sensor from ximea of part number xiQ MQ042CG-CM is placed on the back end of the eye model to capture the projected image from the microdisplay via the model. Hence, the eye and the lens as the optical system for the image sensor. An example of the captured image using the different lenses is shown in Fig. 3. The purpose of this step is to ensure that the image delivered to the retina (image sensor) is focused and has the minimum possible distortion. Then, is substituted with the photodiode UV-818 from Newport to measure the light intensity at the retina surface. The photodiode is connected to the source measuring unit (SMU) from Keithley of number 2612B. In this experiment, the 90x90 µLED matrix described in [9, 17] is used as the microdisplay. Moreover, the details of the experiment, the image processing part and the control algorithm of the headset is published in [14]. A photo for the test platform using different lenses is illustrated in Fig. 3 respectively. The efficiency of the different lenses is calculated by dividing the measured light intensity from each pixel after and before the optical system. The measured optical efficiency for the three lenses; the linear lens, folded prism, and contact lens; is depicted in Fig. 4 (a), (b), and (c) respectively. The average optical efficiency is 10% for the contact lens configuration. On the other hand, the average optical efficiency for the folded prism is 3.5% while for the linear lens is 1.5% as shown in Fig. 4.

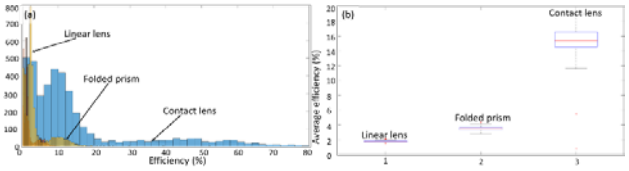


Fig. 4 Measured optical efficiency for the three lenses (a) the efficiency distribution for the different lenses (b) average efficiency for the different lenses.

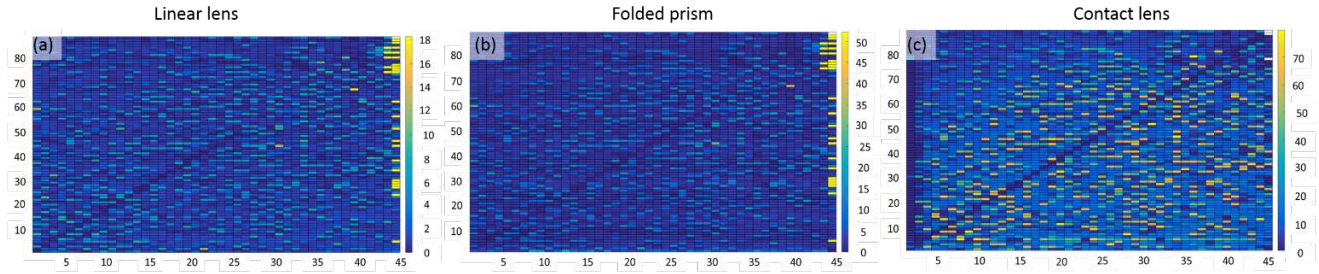


Fig. 5 efficiency distribution of the optical system due to each pixel (a) efficiency distribution for the linear lens which shows the minimum change in the efficiency between adjacent pixels but also the maximum achieved efficiency is 18%. (b) efficiency distribution for the folded prism lens which shows small variations in the efficiency between adjacent pixels compared to the contact lens, (c) the change of efficiency over the contact lens which shows that the high efficiency pixels are located in the middle of the lens but with large variations in the efficiency.

The main reason for the efficiency change between pixels in the curvature surface of the eye and the lens (in case of the contact lens and the folded prism).

Moreover, the efficiency distribution over the lens area for the three lenses is illustrated in Fig. 5. The grids of Fig. 5(c) shows that the efficiency for the contact lens varies from 5% till 80%. Furthermore, the high efficiency points are centered on the center of the lens. Although the pixels in the case of contact lens gives high efficiency, this requires calibration to compensate for this variations in the efficiency. On the other hand, the efficiency distribution for the folded prism lens is depicted in Fig. 5 (b). The efficiency varies from 1% to 50% between pixels. However, the variation between the pixels in the center of the lens is not large which relaxes the requirements on the calibration requirements. The efficiency distribution for the linear lens is illustrated in Fig. 5 (a).

The maximum achieved efficiency for the linear cell is 18% which is the smallest efficiency among the tested lenses. The main reason for the low efficiency for the linear lens is the large distance between the microdisplay and the lens. Yet, the difference in efficiency between pixels is small and hence the calibration step to compensate for the mismatch can be removed. This improves the processing latency of the system in the case of the linear lens. Moreover, the light distribution is more even in the case of the linear lens than the folded prism and contact lenses as illustrated in Fig. 5.

IV. DISCUSSION

In this work a comparison between three different lenses is done in order to design the optimum optical system for a wearable headset to help people with retina pigmentosa to restore vision. The contact lens achieved the highest efficiency compared to the folded prism and linear lenses configurations. Moreover, using the contact lens make the headset small in size. Yet, the main challenge of the contact lens is its weight as its D parameter is 52 which make it heavy to remain on the pupil with this size. Moreover, the folded prism virtual reality lens from eMagin is used to build the system. Indeed, the folded prism lens achieve less efficiency than the contact lens and the headset is larger than in the case of the contact lens. Yet, the headset in this case is independent on the pupil which make it easy to design. Furthermore, the linear lens from oculus rift is also evaluated with the headset which showed the minimum optical efficiency. This is due to the large spacing between the lens and the microdisplay. Also, the headset in case of using the linear lens is the largest in the size compared to the other two types.

On the other hand, the linear lens achieve the minimum variation between pixels. Moreover, the efficiency distribution of the pixels in the middle is similar to each other's. This relaxes the requirements for a calibration step to compensate for the efficiency mismatch. Yet, the low efficiency will lead to driving the pixels with the maximum power in order to achieve the required light threshold for stimulation. Hence, the power requirement for the system in this case is maximized again. The contact lens achieve the maximum average efficiency which is 10%. Hence, the headset does not need to drive the pixels with the maximum power and this achieve power saving for the system. Yet, due to the large variations in the efficiency between pixels, a calibration step is needed to compensate for this mismatch. This increase the complexity of the software for the headset. Indeed, the folded prism lens is the lens which achieve the optimum case for the headset as it achieve good efficiency with also small size compared to the linear lens.

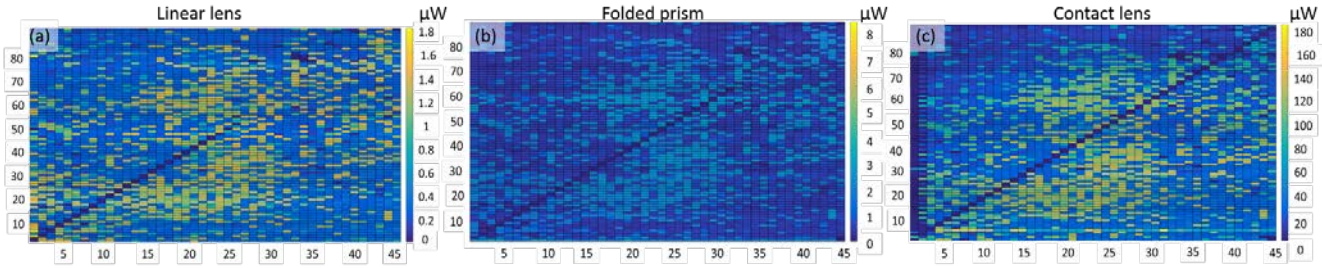


Fig. 6 light power distribution in µW of the optical system at each pixel (a) illumination distribution for the linear lens which shows the minimum change in the light power between adjacent pixels but also the maximum achieved light power is 1.8. (b) illumination distribution for the folded prism lens which shows small variations in the power between adjacent pixels compared to the contact lens, (c) the change of illumination over the contact lens which shows that the high power pixels are located in the middle of the lens but with large variations in the illumination power,

Table I Summary for the number of pixels and the average intensity for each lens for two stimulation thresholds

	Linear lens		Folded prism		Contact lens	
Threshold (mW/mm^2)	0.7	0.1	0.7	0.1	0.7	0.1
Number of pixels	8	3334	1198	3386	3267	3742
Average intensity (mW/mm^2)	0.741	0.278	1.06	0.504	2.46	2.22

In order to achieve stimulation using optogenetics, the light on the retina surface has to be more than $0.7mW/mm^2$ [1]. This is the threshold for optogenetics stimulation. Hence, the received light power at the retina surface is measured to ensure the efficacy of the headset. The measure light power from each pixel at the retina surface (the back end of the eye model and after the optics) is illustrated in Fig. 6. Interestingly, the three lenses are able to generate enough light for stimulation at the retina surface. Yet, the number of the effective pixels (the pixels that deliver enough light for stimulation) varies between the three configurations. The contact lens gives the highest number of effective pixels while the linear lens gives the minimum number of effective pixels. This is because the low efficiency for the linear lens. This impacts the resolution of the image delivered to the retina. Yet, the minimum number of pixels required to achieve an acceptable vision is 1024 pixel which is fulfilled by the three types of the lens for a stimulation threshold of $0.1mW/mm^2$ as listed in Table I. Yet for a $0.7mW/mm^2$, only the contact lens and the folded prism achieve the acceptable resolution while the linear lens only 8 pixels will achieve stimulations as illustrated in Table I.

V. CONCLUSION

In this work, the impact of three different lenses on the performance of a headset for optogenetics based stimulation is characterized. The contact achieved the highest efficiency upto 80% with the smallest size compared to the other two lenses. On the hand, the folded prism lens achieved efficiency upto 50% with the maximum power at the retina surface of 8µW. finally, the linear lens achieved the lowest efficiency of 18% with the maximum power on the retina surface of 1.8µW. the folded prism give headset with smaller size than the linear lens. Yet, the linear lens required less data processing due to the small variations between the different pixels.

VI. ACKNOWLEDGMENT

We would like to thank Prof. Daniel Palanker, Stanford University for advising the use of an eye model to demonstrate that our system could provide sufficient irradiance. We would also like to thank the European Commission for funding the OptoNeuro project (249867) which developed the LED arrays. We would also like to thank the Macular Society for funding work on augmented vision systems for the blind, and the British Council for funding collaboration between the UK and Egypt (216344044). The authors would also like to thank the Wellcome Trust (grant numbers 096975/Z/11/Z, 102037/Z/13/Z), as well as the Engineering and Physical Sciences Research Council (NS/A000026/1) for funding the CANDO (www.cando.ac.uk) project.

REFERENCES

[1] K. Deisseroth, "Optogenetics," *Nature methods*, vol. 8, no. 1, pp. 26--29, 2011.

[2] Ledri, Marco and Madsen, Marita Gr{\o}nning and Nikitidou, Litsa and Kirik, Deniz and Kokaia, Merab, "Global Optogenetic Activation of Inhibitory Interneurons during Epileptiform Activity," *Journal of Neuroscience*, vol. 34, no. 9, pp. 3364--3377, 2014.

[3] G. Nagel, T. Szellas, W. Huhn, S. Kateriya, N. Adeishvili, P. Berthold, et al., "Channelrhodopsin-2, a directly light-gated cation-selective membrane channel," *Proceedings of the National Academy of Sciences*, vol. 100, pp. 13940-13945, 2003.

[4] Dong, N., Berlinguer-Palmini, R., Soltan, A., Ponon, N., O'Neil, A., Travelyan, A., Maaskant, P., Degenaar, P. and Sun, X, "Opto-electro-thermal optimization of photonic probes for optogenetic neural stimulation," *Journal of biophotonics*, p. p.e201700358., 2018.

[5] Yoo, Sunghyun and Lee, Hongkyun and Jun, Sang Beom and Kim, Yong-Kweon and Ji, Chang-Hyeon, "Disposable MEMS optrode array integrated with single LED for neurostimulation," *Sensors and Actuators A: Physical*, vol. 273, pp. 276--284, 2018.

[6] Wang, Lulu and Huang, Kang and Zhong, Cheng and Wang, Liping and Lu, Yi, "Fabrication and modification of implantable optrode arrays for in vivo optogenetic applications," *Biophysics reports*, vol. 4, no. 2, pp. 82--93, 2018.

[7] Zhao, Hubin and Soltan, Ahmed and Maaskant, Pleun and Dong, Na and Sun, Xiaohan and Degenaar, Patrick, "A Scalable Optoelectronic Neural Probe Architecture With Self-Diagnostic Capability," *IEEE Transactions on Circuits and Systems I: Regular Papers*, p. In Press, 2018.

[8] Ramezani, Reza and Liu, Yan and Dehkhoda, Fahimeh and Soltan, Ahmed and Haci, Dorian and Zhao, Hubin and Firfilionis, Dimitrios and Hazra, Anupam and Cunningham, Mark O and Jackson, Andrew and others, "On-Probe Neural Interface ASIC for Combined Electrical Recording and Optogenetic Stimulation," *IEEE transactions on biomedical circuits and systems*, 2018.

[9] A. Soltan, B. McGovern, E. Drakakis, M. Neil, P. Maaskant, M. Akhter, et al, "High Density, High Radiance micro-LED Matrix for Optogenetic Retinal Prostheses and Planar Neural Stimulation," *IEEE Transactions on Biomedical Circuits and Systems*, vol. 11, pp. 347-359, 2017.

[10] Hong, In Yeol and Lee, Jae Hyeok and Cho, Sung Min and So, Jae Bong and Kim, Tae Kyoung and Cha, Yu-Jung and Kwak, Joon Seop, "Impact of Hydrothermally Grown ZnO Nanorods on External Quantum Efficiency of 32$\times$ 32 Pixelated InGaN/GaN Micro-LED Array," *IEEE Transactions on Nanotechnology*, vol. 18, pp. 160--166, 2019.

[11] Soltan A, Passetti G, Maaskant P, Degenaar P., "High density µLED array for retinal prothesis with a eye-tracking system.," in *Biomedical Circuits and Systems Conference (BioCAS)*, 2016.

[12] B. Thylefors, A. D. Negrel, R. Pararajasegaram, and K. Y. Dadzie, "Global data on blindness," *Bulletin of the world health organization*, vol. 73, p. 115, 1995.

[13] L. da Cruz, J. D. Dorn, M. S. Humayun, G. Dagnelie, J. Handa, P. O. Barale, et al., "Five-Year Safety and Performance Results from the Argus II Retinal Prosthesis System Clinical Trial," *Ophthalmology*, vol. 123, pp. 2248-2254, 2016.

[14] Ahmed Soltan, John Barrett, Pleun Maaskant, Niall Armstrong, Walid Al Atabany, Lionel Chaudet, Mark Neil, Evelyne Sernagor, Patrick Degenaar, "A Head Mounted Device Stimulator for Optogenetic Retinal Prosthesis," *Journal of Neural Engineering*, vol. 15, no. 6, p. 065002, 2018.

[15] D. W. Cheng, Y. T. Wang, H. Hua, and M. M. Talha, "Design of an optical see-through head-mounted display with a low f-number and large field of view using a freeform prism," *Applied Optics*, vol. 48, pp. 2655-2668, 2009.

[16] Foerster, Rebecca M and Poth, Christian H and Behler, Christian and Botsch, Mario and Schneider, Werner X, "Using the virtual reality device Oculus Rift for neuropsychological assessment of visual processing capabilities," *Scientific reports*, vol. 6, p. 37016, 2016.

[17] A. Soltan, H. Zhao, L. Chaudet, M. Neil, P. Maaskant, and P. Degenaar, "An 8100 pixel optoelectronic array for optogenetic retinal prosthesis," *in 2014 IEEE Biomedical Circuits and Systems Conference (BioCAS) Proceedings*, pp. 352-355, 2014.