33rd Annual International Conference of the IEEE EMBS
Boston, Massachusetts USA, August 30 - September 3, 2011

Ultra-High Photosensitivity Silicon Nanophotonics for Retinal Prosthesis: Electrical Characteristics

Massoud L Khraiche[1], Yuhwa Lo[2], Deli Wang[3], Gert Cauwenberghs[4], William Freeman[5] and Gabriel A. Silva[6].

Abstract— **Retinal degenerative diseases such as age related macular degeneration (AMD) and retinitis pigmentosa (RP), lead to the loss of the photoreceptor cells rendering the retina incapable of detecting light. Several engineering approaches have aimed at replacing the function of the photoreceptors by detecting light via an external camera or photodiodes and electrically stimulating the remaining retinal tissue to restore vision. These devices rely heavily on off-device processing to solve the computational challenge of matching the performance of the PRs. In this work, we present a unique ultra-high sensitivity photodetector technology with light sensitivity, signal amplification, light adaptation that shows signal transduction performance approaching those of the rods and cones in the mammalian retina. In addition, the technology offers nanoscale control over photodetectors topography with the potential to reproduce the visual acuity of the natural retina. This technology promises to drastically reduce the foot print, power consumption and computational needs of the current retinal prothesis, while reproducing high resolution vision.**

I. Introduction

The world health organization reports about 314 million people worldwide are visually impaired and 45 million are clinically blind. The causes for blindness vary greatly, and include retinal degenerative diseases as well as traumatic injury as candidates for prosthetic intervention.

The retina is an extension of the central nervous system in the eye. For the retina, in healthy tissue, the PRs modulate the release of neurotransmitters in response to light and stimulate the bipolar and horizontal cell layers which in turn stimulate the ganglion cell layer that possess axonal extensions leading all the way to the brain. Loss of photoreceptors in the retina due to diseases such as age related macular degeneration and retinitis pigmentosa (RP) renders the retina incapable of detecting light, on the other hand the surrounding neural tissue may be intact and still responsive to stimulation [1].

Charles LeRoy was the first to show in 1755 that current stimulation of the retina can produce visual percepts in blind patients. Neurons can be excited via current stimulation by driving a current through neural tissue. The stimulation typically is a biphasic current waveform for the purpose of driving a constant current through the tissue and then driving the reverse current to maintain charge balance. This has led to several efforts aimed at engineering an implantable device that could replace the function of the degenerated photoreceptors by detecting light and properly stimulating retinal neurons [1,2, 3]. These types of devices interaface with the retina from either the Subretina side (to stimulate bipolar and horizontal cells) or the Epiretina side (to stimulate the ganglion cells).

Currently, most retinal prosthetics can be divided into two types based on the method of light detection. The first type which is adapted by leading groups across the United States rely on an external camera for image capture and processing elements to determine proper retinal stimulation. This approach does not make use of the eye's natural ability to locate and follow objects and includes added components (camera and processing hardware) which increase the size, weight and power consumption of the overall device. The second type of retinal prosthesis relies on microphotodiodes for light detection and stimulation. This approach lack sufficient current output to successfully stimulate the retina which requires added on-chip analog amplifiers and large photosensitive surface which limits the overall resolution of the implant [3].

In this work, we propose the use of silicon nanophotonic to replace the light sensing and signal transduction functions of PRs. This technology relies on semiconductor vertical nanowires developed by our group as high sensitivity, low power and broadband photodetectors. These semiconductor silicon nanowire arrays are made from Epi silicon (p+/p-/p +). The electrical conductivity of semiconductors changes when they absorb light with enough energy to excite an electron-hole pair. The large surface to volume ratio gives rise to the high intrinsic gain by depletion of the holes in the p- region of the NW (Fermi pinning) [4,5,6,7,8]. The nanowires provide an ideal replacement for photoreceptors due to near single photon sensitivity, and the ability to tailor the size and spatial distribution of the nanowires arrays. We will present the characteristics of the nanowire and how that compares to those of the PRs in the eye.

II. Materials and Methods

A.Fabrication of the nanowires

Photoresist nano islands are imprinted on Epi silicon wafer (p+/p-/p+) over another layer of photoresist. The nano-imprinting technique offers a quick and cost effective method of patterning nano-structures and is previously published by our group [8]. Dry reactive ion etching (RIE) is used to remove the second layer. Nickel (Ni) is deposited by evaporation (Thickness = 80nm) and the nano islands are lifted off. The Ni is used as mask for etching the silicon via reactive ion etching (RIE) and followed by annealing the Ni for hour at 650^{o}C. The insulations of the array is done by spin coating PDMS and baking for 5 minutes over 80^{o}C and RIE is used to etch until tips of the nanowires are exposed (Fig. 1). The etched nanowires were 200nm in diameter with varying island sizes. The transparent top contact used for biasing the nanowires was formed by depositing indium tin oxide (ITO).

1, 4, 5 Department of Bioengineering, University of California, San Diego, CA
6 Jacobs Retina Center, San Diego, CA
2, 3 Department of Electrical and Computer Engineering, University of California, San Diego, CA

B.Setup

The setup for testing the nanowires is shown in Fig. 2. Incident light over an area of 1um^2 produced from an attenuated red (635 nm) diode laser. Light intensities used to stimulate the nanowires were 1 µW/mm^2 (unless otherwise mentioned). Chopper was used to modulate the light at a 100Hz frequency in some cases. For testing in fluid, the nanowires were immersed in ringer's solution (in mM): 117 NaCl; 3.0 KCl, 2.0 CaC l2, 1.0 $MgSO_4$, 0.5 NaH_2PO_4, 15.0 D-glucose, 32 $NaHCO_3$.

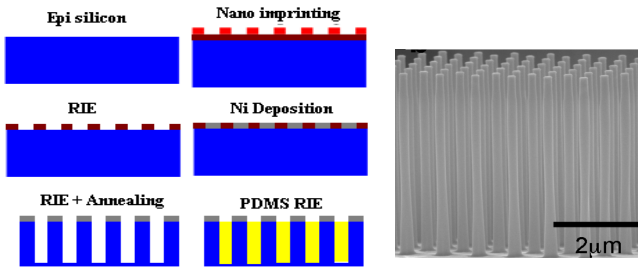

Fig. 1: Left, the process flow of silicon nanowire photodetectors starting with p+/p-/p+ silicon. Right, SEM of the etched nanowires

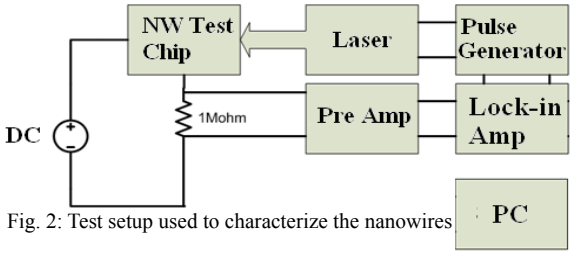

Fig. 2: Test setup used to characterize the nanowires

C. Neuron cultures

Cortical slices from embryonic, day 18, Sprague/Dawley rat were obtained from Brainbits (Springfield, IL). NW chips were autoclaved and coated with poly-D-lysine (PDL) and laminin (Sigma, USA). Neurons were seeded on the chips after enzimatic digestion of the cortical slice. Cells were grown in Nbactive4 media, also obtained from Brainbits (Springfield, IL) [14]. Neurons were labeled with a Live/ Dead (calcein/ethidium homodimer) assay (invitrogen, USA).

III. Results and Discussion

Our research efforts here are focused on the novel characteristics of silicon nanowires that are particularly relevant and attractive to replace the function of the photoreceptors. These characteristics are elucidated in the following as guidelines for any new technology that holds promise to replace the damaged photoreceptors;

A. Topography control

Functional organization of the photoreceptors in the retina provides a challenge for prosthetic devices aimed at replacing the retina's ability to detect light with high visual acuity. An example of this specialized organization of the PR is the fovea, which owes its high visual acuity to the ratio of ganglion cells to PRs (can be one to one). The density of cones in human retina range between 90,000 -300,000 cones/mm^2 while rods can reach 179,000 rods/mm^2 and decrease by around 10-15% across the retina. In addition to the distribution, rods and cones have a range of height between 40-50 µm long and their diameter varies between . 50 to 4.0 µm. The size of the PRs and their density also provide a specialization since it govern photon interaction areas. The advantage of using nanoimprinting to manufacture the nanowire array provides control over spatial distribution and form factor. This allows for control over spacing between the nanowires down to 2nm, diameters ranging between 200nm-5µm, and length ranging between 1-50 µm. This enables tailoring the nanowires to fit the distribution of the PRs they are replacing.

B. Phototransduction

Both rods and cones are capable of phototransduction. In short, PRs respond to light stimulation by changing their membrane potential to a more hyperpolarized state which alters the release of neurotransmitters. In parallel, the nanowires are capable of phototransduction and are well documented as high sensitivity photodetectors by our group [11]. The holes in the p- region of the (p+/p-/p+) nanowires are all depleted from the center and trapped in the surface states. When visible light illuminates the nanowires, electron-hole pairs are generated. Electrons are instantly driven to the surface leaving the holes in the center of nanowires (Fig. 3). As a result, the originally insulated nanowires become electrically conductive for the duration before the holes in the nanowires are finally trapped to the surface again, which might take <1 us to 1 ms depending on the intensity of light. This is far more superior to the res-

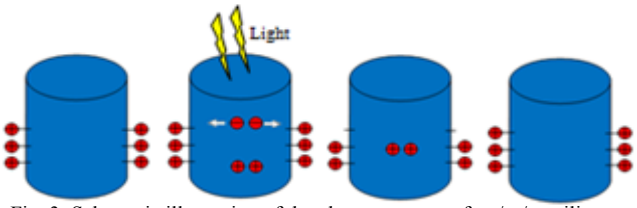

Fig. 3: Schematic illustration of the photo response of p+/p-/p+ silicon nanowire detector.

-ponse time of 70-120 ms of rods and cones (depending on background illumination) [12]. Without illumination, the nanowires behave as insulators because all mobile charges (i.e. holes) in the nanowires are completely depleted. In addition, increasing light intensity increases the photocurrent (Fig. 4).

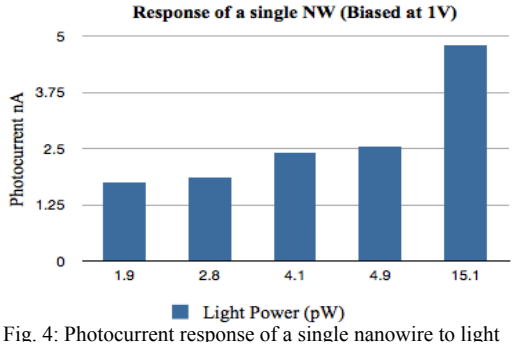

Fig. 4: Photocurrent response of a single nanowire to light

C. Light adaptation and amplification

The rods and cones can operate on an extremely large range of illumination (lowest 10-100 lux). This is owed to light responsive ion channels and also to neural interactions between horizontal cells and photoreceptor terminals contribute to the reduction of amplification with increasing light intensity. The nanowires can be made to mimic this control via feedback control that governs the level of bias voltage. Looking back to Fig. 5, the photocurrent response can be changed by changing the voltage applied to the nanowires, providing control over the output. In addition, the nanowires can respond to light as low as 0.1 fW (10-16 W), corresponding to illumination of (6-10 lux).

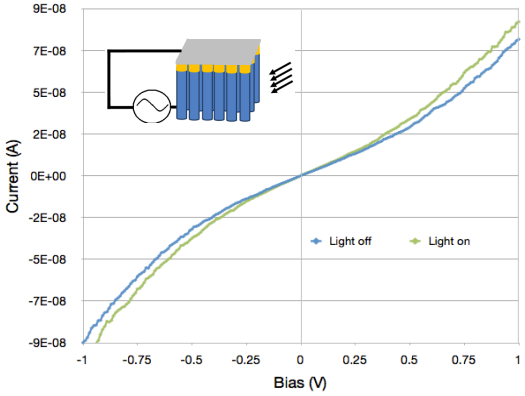

Fig. 5: IV curve of a 10X10 Nanowire array under light stimulation at room temperature.

D. Neural stimulation

The PRs stimulate neural tissue via the release of neurotransmitters. Neurons can also be excited via current stimulation by driving a current through neural tissue. Typically, the current waveform for neural stimulation is monophasic or biphasic current pulse. The amount of charge needed to stimulate the retina is around 1uC, delivered over 5 msec, with a charge density of 1mC/cm2. Current used for stimulation = 200uA, with max frequency = 100Hz. The nanowires produce a photcurrent in response to light stimulation which can be modulated by the applied bias Fig. 5. Results in Fig.3 show that Nanowires platform capable of producing current levels and waveforms sufficient for neural stimulation, the proposed setup for stimulation is shown in Fig.6. The photocurrent produced by the nanowires can be used to inject current into the retina when placed near the tissue. Rat retina will be removed and place a microelectrode array with the Epiretina side facing the recoding sites while the nanowire array will face the Subretina side. Retina activity will be recorded via a Microelectrode arrays. The IV curve in Fig. 2 shows nanowire response in setup similar to Fig.6, where the ground is a distance away from the array and the bias is applied across the neural recording solution.

Looking to Fig.8 its clear dark current plays a large role in the IV curve of the nanowire array. The performance of photoconductive nanowires can be improved by n-doping the p- region to reduce the reliance on surface state to trap the holes. This would produce a better performance in room temperature or fluid and reduces the dark current.

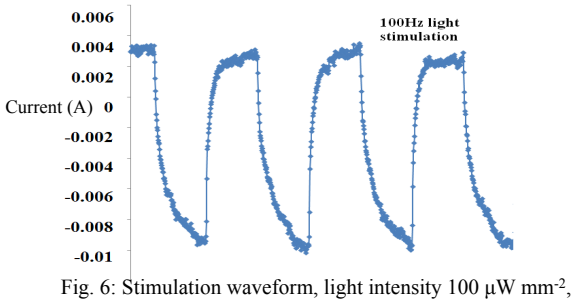

Fig. 6: Stimulation waveform, light intensity 100 µW mm^{-2},

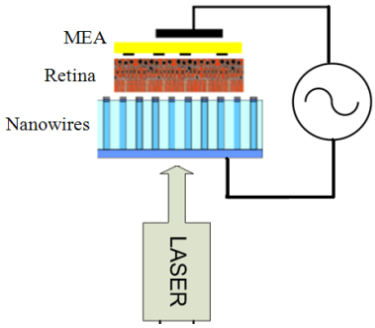

Fig. 7: shows setup for testing the potential for neural stimulation capabilities of the nanowire platform.

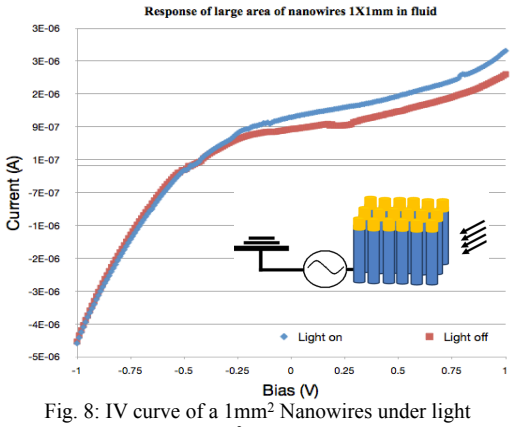

Fig. 8: IV curve of a 1mm^2 Nanowires under light stimulation 1 µW mm^{-2} in fluid (ringer's solution).

E. Biocompatibility

Nanotopography has been shown to improve tissue integration of prosthetic devices and even recovery from injury [12]. This should reduce the amount of current needed to stimulate neural tissue which would minimize power consumption of the prosthetic device and resulting tissue damage. The nanowire platform that we designed has an inherit nanotopography which would interface directly with the ganglion cells in a setup similar to the one in Fig.7. Another advantage for using the nanowires to interface with the retina is that nanotopography has been shown to improve tissue integration of prosthetic devices. In fact, recent work has shown that using nanotopography at the site of stimulation reduces the amount of current needed to stimulate neural tissue which would minimize power

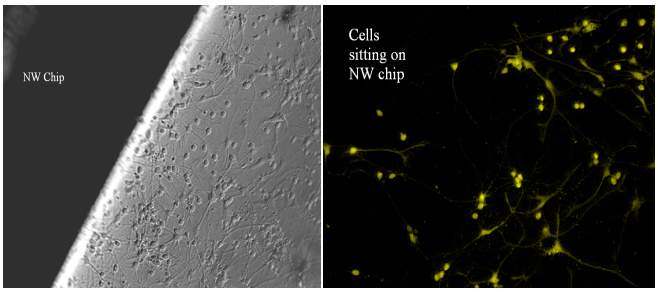

Fig. 9: A) Rat cortical cultures were grown around the nanowire array, B) Rat cortical cultures stained with a L/D assay (green live) growing on the nanowire substrate

consumption of the prosthetic device and resulting tissue damage. Finally, we have done some initial cytotoxicity tests to show that the fabrication of the nanowire chips has no toxic effect on cortical cultures (Fig.9).

IV. Conclusions and Future Work

The presented body of work shows the proposed technology carries a lot of promise for application in a prosthetic platform to replace the function of the PRs. Future work needs to explore core shell approaches to reducing the dark current by relying on doping to improve trapping holes at room temperature.

The long term aims of our group is to produce a nanoengineered retinal prosthesis capable of tissue integration on a scale comparable to those of proteins and lipids, with light sensing and stimulation elements near rod and cons light sensitivity and spatial distribution. Also, the choice of the nanowires for light detection provides on-device wireless image capture and eliminates the need for an external camera. This coupled with inductive telemetry for wireless power delivery provides a wireless minimally invasive implant, highly integrated without internal wiring on a miniature flexible substrate.

Acknowledgment

The authors would like to acknowledge Hasan Mohammad Faraby, Arthur Zhang and James Cheng for their help with some of the experimental setups.

References

[1] Winter, J., S. Cogan, and J. Rizzo, *Retinal prostheses: current challenges and future outlook.* Journal of Biomaterials Science, Polymer Edition, 2007. 18: p. 1031-1055.

[2] Humayun, M.S., et al., *Visual perception in a blind subject with a chronic microelectronic retinal prosthesis.* Vision Res, 2003. 43(24): p. 2573-81.

[3] Besch, D., et al., *Extraocular surgery for implantation of an active subretinal visual prosthesis with external connections: feasibility and outcome in seven patients.* Br J Ophthalmol, 2008. 92(10): p. 1361-8.

[4] Zhang, A., et al., *Nanowire Photodetectors.* Journal of Nanoscience and Nanotechnology, 2010. 10: p. 1430-1449.

[5] Zhang, A., et al., *Characterization and physics of top-down silicon nanowire phototransistors.* Proceedings of SPIE, 2010. 7608: p. 76081D-8.

[6] Sun, K., et al., *Compound Semiconductor Nanowire Solar Cells.* Selected Topics in Quantum Electronics, IEEE Journal of, 2010. PP(99): p. 1-17.

[7] Soci, C., et al., *ZnO Nanowire UV Photodetectors with High Internal Gain.* Nano Letters, 2007. **7**(4): p. 1003-1009.

[8] Kim, H., A. Zhang, and Y. Lo, *Fabrication of Vertical Silicon Nanowire Photodetector Arrays using Nanoimprint Lithography.* Proceedings of SPIE, 2010. 7591: p. 7591-5.

[9] Soci, C., et al., *Nanowire Photodetectors.* Journal of Nanoscience and Nanotechnology, 2010. **10**(3): p. 1439-1449.

[10] Curcio, C.A., et al., *Human photoreceptor topography.* J Comp Neurol, 1990. **292**(4): p. 497-523.

[11] Zhang, A., et al., *Silicon nanowire detectors showing phototransistive gain.* Appl. Phys. Lett., 2008. **93**(12): p. 121110.

[12] Friedburg, C., M.M. Thomas, and T.D. Lamb, *Time course of the flash response of dark- and light-adapted human rod photoreceptors derived from the electroretinogram.* J Physiol, 2001. 534(Pt 1): p. 217-42.

[13] Palanker, D., et al., *Design of a high-resolution optoelectronic retinal prosthesis.* J Neural Eng, 2005. 2 (1): p. S105-20.

[14] Khraiche, M.L., N. Jackson, and J. Muthuswamy. *Biology Society, 2009. EMBC 2009. Annual International Conference of the IEEE*. 2009.