Modeling and Evaluating Prima Implant with Pulse2Percept

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ABSTRACT

In this paper, we model the Prima implant and investigate its performance for restoring sight to patients suffering from degenerative diseases such as retinitis pigmentosa. In particular, we present a strategy for simulating the essential features of the implant using primatives provided by *pulse2percept*, a framework for modeling bionic vision implants. Additionally we evaluate the implant against existing retinal and subretinal implants such as AlphaIMS and Argus II and we compare its performance on the basis of functional resolution (as determined by principle component analysis) as well as image quality across a range of test stimulus patterns. Our results show that the Prima implant is highly efficient in terms of the number of functional electrodes it produces as a percentage of the total resolution of the implant, but it may leave room for improvement especially when evaluated implants with higher densities of electrodes.

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Figure 1: Diagram of an Electrode from the Prima implant from the paper *Optimization of return electrodes in neurostimulating arrays* [7]

INTRODUCTION

Prima is a next generation subretinal implant for restoring sight to patients suffering from conditions such as retinitis pigmentosa. It is noteworthy for its relatively high density array consisting of 378 electrodes (100 μm electrodes with 5μm trenches [9]) as well as its interesting activation strategy. The electrodes in the Prima implant are activated using an infrared projector that illuminates the implant with the desired stimulation pattern. This light serves to both power the implant and determine which electrodes should activate. It is hoped that this strategy will allow for simpler surgeries to implant the device at the cost of a more complex optical power delivery and stimulation system. In this paper we look at both the challenges related to simulating Prima in software, as well as the performance of a simulated Prima implant in relation to other retinal implants:

- *Argus II*: Argus II is an epiretinal implant situated on the retina designed to help patients with retinitis pigmentosa. The implant consists of an electrode array with 60 electrodes.[6]
- *Alpha AMS*: Alpha AMS is a subretinal implant that aims to help patients with retinitis pigmentosa. The implant consists of an electrode array with 1600 electrodes (40 by 40). [5]

In our study, we hope to answer the following research questions:

(1) How does the Prima implant compare to other bionic implants in terms of effective electrodes?
(2) How, if at all, does the use of Hexagonal Electrodes affect the quantitative quality of the image generated by the Prima implant in relation to other implants?

RELATED WORK

In the original PRIMA paper [8] the authors propose the structure of an implant using a hexagonal array of electrodes powered by pulsed light projected into the eye. This paper explains the design of the implant and covers an evaluation of its performance *in vivo*. [8] describes the design of the electrodes used in Prima as consisting of a central 20 μm disk surrounded by a hexagonal return electrode. The hexagonal electrode assemblies used measure 70 μm across with 5 μm trenches between them. The electrodes themselves are composed of photodiodes which create flow from the active electrodes to the return electrodes when they are illuminated. The authors claim that the use of these

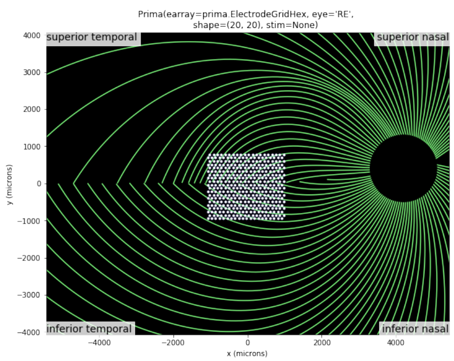

Figure 2: Layout of the Hexagonal electrode grid

return electrodes allows them to tightly confine the electric field they use for stimulus, this is not currently included in our model but is something we would like to account for in future work.

In the paper [7] the authors look at optimizing the structure of hexagonal electrodes of the same design as those used in the Prima implant. They do this by modeling the properties of the electrodes in software, and running simulations of an electrode array to optimize the electrode configuration. This paper goes into detail about the structure of the electrodes used in the Prima implant. Through their simulations the authors found that, while standard dense electrode configurations tend to leak voltage along axon fibers resulting in streaks, by creating a mesh of interconnected return electrodes in the Prima implant the stimulating electric field can be more confined. This means that the retinal cells can be targeted while avoiding accidental stimulation of the ganglion layer. This result informs our decision to evaluate the Prima implant using a Scoreboard model rather than the AxonMap model used by retinal implants such as Argus II.

The authors of [3] present an interesting methodology for quantitatively measuring the quality of implants using principal component analysis (PCA). The authors generate percepts for each distinct electrode in the devices they test and then measure the number of principal components necessary to explain 95% of the variance. They argue that this can be considered a good metric for the number of 'effective electrodes' [3] in the device. We adopt this methodology to evaluate the Prima implant with respect to the Argus II and AlphaAMS devices.

IMPLEMENTATION

Implant Design

We chose to model the Prima device as it was implanted in the 2017 clinical trials[9] by Pixum Vision (the developers of the implant). The Prima implant used in the trial consisted of a grid of 378 electrodes measuring approximately 2mm by 2mm. Based on our literature review, we believe that the hexagonal electrodes used in this version of the implant were $100\mu m$ across. Additionally, each $100\mu m$ electrode is comprised of an active electrode at its center (approximately $20\mu m$ across) surrounded by a return electrode [7] [4].

In Figure 1 you can see a diagram of the layout of a single electrode of the Prima implant found in the paper *Optimization of return electrodes in neurostimulating arrays* [7]. The disk marked 1 in the diagram is the active electrode, it is surrounded by the return electrode marked 2. The intent of the return electrode is to reduce the spread of current through fluid in the eye.

As shown in Figure 2, the unconventional hexagonal electrode shape lends itself nicely to a denser packing of electrodes, but it presents some difficulty for simulation.

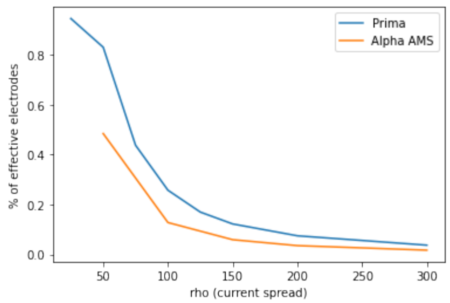

Figure 3: Prima vs. Alpha AMS: Percentage of Effective Electrodes With Changing Rho

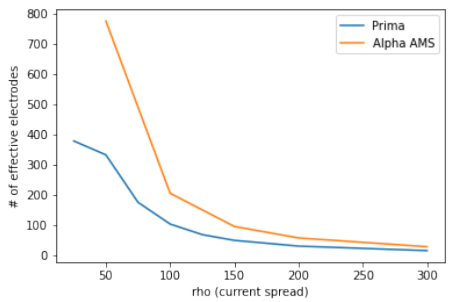

Figure 4: Prima vs. Alpha AMS: Number of Effective Electrodes With Changing Rho

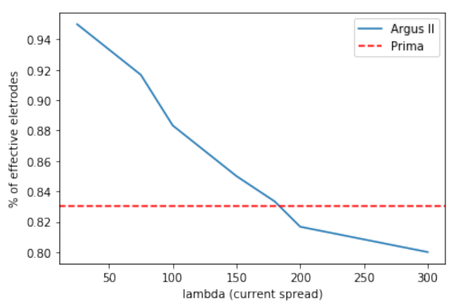

Figure 5: Prima vs. Argus: PCA Components With Changing Lambda

Simulation Strategy

To implement Prima we make a number of simplifying assumptions. Firstly, as we believe the overall shape of the implant is less important than its size and layout, we approximate its unconventional shape (consisting of 378 electrodes) by rounding the number of electrodes in the implant up to 400 and making the implant a hexagonal grid of 20 by 20 electrodes. Secondly, the electrodes themselves used by Prima are hexagonal, however the math to accurately model how electricity spreads out from a hexagonal electrode is quite complex. We instead model them instead as much simpler disk electrodes which are provided by the Pulse2Percept [1].

To model the Prima implant we began by extending pulse2percept with a new class supporting Prima's unique hexagonal electrode grid layout. We subclass the framework's provided ElectrodeGrid class, which represents an organized grid of electrodes, and extend it with a new hexagonal grid layout that better matches the organization and spacing used by Prima. With this generalized component we then implement the Prima implant by instantiating a hexagonal elctrode grid of 20 by 20 disk electrodes measuring 20 μm cross with a spacing of 100 μm. We model only the active portions of the electrodes and choose this 100μm spacing to accurately represent the size of the hexagonal assemblies.

EVALUATION

To evaluate PRIMA, we compare PRIMA to Alpha AMS, another sub-retinal implant[8, 11], and to Argus II, a retinal implant [10]. Because PRIMA and Alpha AMS are sub-retinal implants, we use the scoreboard model. For the Argus II implant we use a axon map model. The scoreboard model has a ρ parameter, and the axon map model has both ρ and λ parameters. The ρ parameter is an exponential decay constant for current away from the axon. The λ parameter is an exponential decay constant for current along the axon [2].

Measuring Effective Electrodes in Bionic Implants

We adopt the methodology from [3] to measure the number of effective independent electrodes in the implants we tested. For each implant, we stimulate each electrode independently in our corresponding implants. Stimulating all of its N electrodes independently results in an N dimensional space of possible percepts. We then estimate the number of effective electrodes to be the number required to explain 95% of the variance in the percepts. We compute this using Principle Component Analysis (PCA).

Experiment Settings. Since PRIMA and Alpha AMS are both subretinal implants, we are able to compare the two directly using the scoreboard model defined in Pulse2Percept. To compare the two, we sample different values of rho (50μm - 300μm), and plot the *percentage* of effective electrodes with their corresponding rho values shown in figure 3. Additionally, we plot the *number* of effective

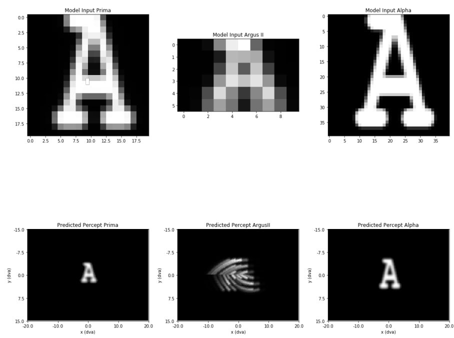

Figure 6: Inputs and predicted percepts for the letter A

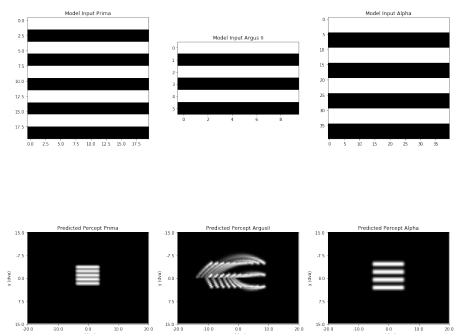

Figure 7: Inputs and predicted percepts for horizontal grating

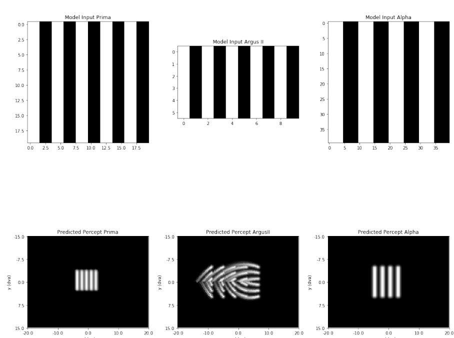

Figure 8: Inputs and predicted percepts for vertical grating

electrodes with their corresponding rho values shown in figure 4. The percentage of effective electrodes is found by:

$$\frac{\#\ of\ principle\ components\ that\ explain\ 95\%\ of\ the\ data}{total\ \#\ of\ independently\ acting\ electrodes}$$

For Argus II, we observe that the number of PCA components has little change with respect to rho, and more heavily depends on changes in lambda. Thus, in our experiments, we vary only the lambda values for Argus II.

We keep the rho value at a constant 50μm for both PRIMA and Argus II. We then plot the percentage of effective electrodes with their corresponding lambda value for Argus II, and depict this in figure 5. To compare Argus II and PRIMA, we plot the percentage of effective electrodes in PRIMA with the same rho value, shown as a dashed line in figure 5.

Results. Interestingly, when comparing Alpha AMS and Prima in figure 3 for when rho value is 50μm, we observe that the percentage of electrodes that are effective for Alpha AMS is 48.3% whereas the percentage of electrodes effective for Prima is 94.5%. This shows that Prima has a higher percentage of working electrodes than Alpha AMS; however when looking at figure 4, because Alpha AMS has a higher number of effective electrodes overall, this could explan why Alpha AMS exhibits higher overall resolution than Prima. We explore this in more detail in the next section.

When comparing Argus II to Prima as shown in figure5, we find that Argus II performs worse than Prima after a lambda value of around 180. Because Prima does not use axonal stimulations, we can not compare changes in lambda.

Comparison of the Percepts Produced by Each Implant

We conduct a series of experiments to compare the precepts generated by each implant. These comparisons are designed to answer the question: How, if at all, does the use of Hexagonal Electrodes affect the quantitative quality of the image generated by the Prima implant in relation to other implants?

Experiment Settings. For the Prima implant and the Alpha AMS implant, we use a scoreboard model with the ρ parameter set to 100μm. For the Argus II implant, we use the axon map model, and set the ρ parameter to 100μm and λ parameter to 200μm.

To conduct our study, we use three black and white images as input to each implant:

(1) The letter A down sampled to the size of the electrode grid.
(2) A vertical grating pattern with the line widths of size: $\lfloor width\ of\ electrode\ grid/8 \rfloor$
(3) A horizontal grating pattern with the line widths of size: $\lfloor height\ of\ electrode\ grid/8 \rfloor$

The simulations for each implant consisted of these three images directly converted to voltage.

Results. We find a significant improvement in the predicted percept resolution for the Prima implant as compared to the Argus II implant. Figures 6, 7 and 7 show that for all three inputs to the Argus II implant, identifying the original input from the predicted percepts is difficult. Additionally, we observe that for Argus II, the predicted percepts are streaky. Contrastingly, Figures 6, 7 and 7 show that for all three inputs to the Prima implant, we can clearly identify the original input from the predicted percepts.

Compared to the Alpha AMS implant, the Prima implant has slightly worse predicted percept resolution. We can see this slight difference in resolution in Figure 2 and 3 where the horizontal and vertical gratings are more clear for the Alpha AMS implant.

The difference in the predicted percept resolution between the three implants can be explained by the difference in number of electrodes in each implant. The Argus II implant has 60 electrodes, the Prima implant has 400 electodes and the Alpha AMS implant has 1600 electrodes. These predictions suggest that with a greater number of electrodes we can generate more meaningful images from percepts. The percepts appear to be streaky for the Argus II implant because of the axon map model.[2]

Limitations and Futurework

As part of our future work we would like to more accurately model the effects of the return electrodes placed around the active disk electrodes in the Prima implant. The return electrode likely has the effect of reducing current spread out from the active electrode which may actually improve the performance of Prima relative to other implants.

Additionally, in this study we used pulse2percept 2.0 which does not yet have support for more advanced stimulus such as pulsetrains. Because of this, we were unable to experiment more thoroughly the visual acuities of the Prima implant. In the future, we would be interested to integrate the effects of different types of stimulus into our comparison, particularly stimulus in gratings as dicussed in [8].

Conclusion

In this study, we leverage the Pulse2Percept framework for simulating bionic vision implants to model the Prima implant. We then evaluate the Prima implant against two well known bionic vision implants: Argus II, a epirentinal implant, and Alpha AMS, a subretinal implant; and compare Prima's peformance in terms of the quality of its predicted percepts and its number of effective electrodes. We find that the Prima implant is highly efficient in terms of the number of functional electrodes it produces as a percentage of the total resolution of the implant, but it may leave room for improvement especially when evaluated with implants that have even higher densities of electrodes such as Alpha AMS.

REFERENCES

[1] Michael Beyeler, Geoffrey M. Boynton, Ione Fine, and Ariel Rokem. 2017. pulse2percept: A Python-based simulation framework for bionic vision. *bioRxiv* (2017). https://doi.org/10.1101/148015 arXiv:https://www.biorxiv.org/content/early/2017/07/10/148015.full.pdf

[2] Michael Beyeler, Devyani Nanduri, James D. Weiland, Ariel Rokem, Geoffrey M. Boynton, and Ione Fine. 2019. A model of ganglion axon pathways accounts for percepts elicited by retinal implants. *Scientific Reports volume* 9, 9199 (jun 2019). https://doi.org/10.1038/s41598-019-45416-4

[3] Michael Beyeler, Ariel Rokem, Geoffrey M Boynton, and Ione Fine. 2017. Learning to see again: biological constraints on cortical plasticity and the implications for sight restoration technologies. *Journal of Neural Engineering* 14, 5 (aug 2017), 051003. https://doi.org/10.1088/1741-2552/aa795e

[4] Edison. 2018. *Encouraging signs in Prima EU feasibility study*. https://www.edisongroup.com/wp-content/uploads/2018/12/Pixium-Vision-Encouraging-signs-in-Prima-EU-feasibility-study.pdf

[5] Thomas L Edwards, Charles L Cottriall, Kanmin Xue, Matthew P Simunovic, James D Ramsden, Eberhart Zrenner, and Robert E MacLaren. 2018. Assessment of the Electronic Retinal Implant Alpha AMS in Restoring Vision to Blind Patients with End-Stage Retinitis Pigmentosa. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5818267/

[6] Avni P Finn, Dilraj S Grewal, and Lejla Vajzovic. 2018. Argus II retinal prosthesis system: a review of patient selection criteria, surgical considerations, and post-operative outcomes. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6005308/

[7] Thomas Flores, Georges Goetz, Xin Lei, and Daniel Palanker. 2016. Optimization of return electrodes in neurostimulating arrays. *Journal of neural engineering* 13 (04 2016), 036010. https://doi.org/10.1088/1741-2560/13/3/036010

[8] Henri Lorach, Georges Goetz, Richard Smith, Xin Lei, Yossi Mandel, Theodore Kamins, Keith Mathieson, Philip Huie, James Harris, Alexander Sher, and Daniel Palanker. 2015. Photovoltaic restoration of sight with high visual acuity. *Nature Medicine* 21, 9199 (Apr 2015), 476–482. https://doi.org/10.1038/nm.3851

[9] Pixium Vision. 2017. *Feasibility Study of Compensation for Blindness With the PRIMA System in Patients With Dry Age Related Macular Degeneration (PRIMA FS)*. https://www.clinicaltrials.gov/ct2/show/NCT03333954

[10] David D. Zhou, Jessy D. Dorn, and Robert J. Greenberg. 2013. The Argus® II retinal prosthesis system: An overview. *2013 IEEE International Conference on Multimedia and Expo Workshops (ICMEW)* (jul 2013). https://doi.org/10.1109/ICMEW.2013.6618428

[11] Eberhart Zrenner, Karl Ulrich Bartz-Schmidt, Dorothea Besch, Florian Gekeler, Assen Koitschev, Helmut G. Sachs, and Katarina. 2016. The Subretinal Implant ALPHA: Implantation and Functional Results. https://doi.org/10.1007/978-3-319-41876-6_6