Cones and Rods - Tianyu

Hypothesis

We have two kinds of vision cells in our retina, cones, and rods, which cones are focused on detecting color and rods work on the brightness. Scientists developed a method that can scan the retina cells when people are still alive, called Adaptive Optics Scanning Laser Ophthalmoscope.
The broader view of the research hypothesis is to find a way using a Deep Neural Network to distinguish the cone cells and the rod cells in an AO-SLO image. However I am a part of it, the narrower view of my work hypothesis, is to follow Dr. David Cunefare's research, use the same way to generate training samples, and build the Convolutional Neural Network to check whether it is feasible.

Background Research

The core research is Dr.Cunefare's work. The first step is to mark the Cones in the AO-SLO images. And what is important is to find the none-Cone samples. Dr. Cunefare introduced a concept called "Voronoi edge", which is the perpendicular bisector of the line segment which connects two adjacent cone centers. Therefore the non-cone samples are randomly chosen from the points on the Voronoi edges. For each sample point, Dr. Cunefare pick a 33*33 pixel patch around the sample point as an input sample for the Neural Network. In total, the ratio of cone and non-cone samples is 4:6.

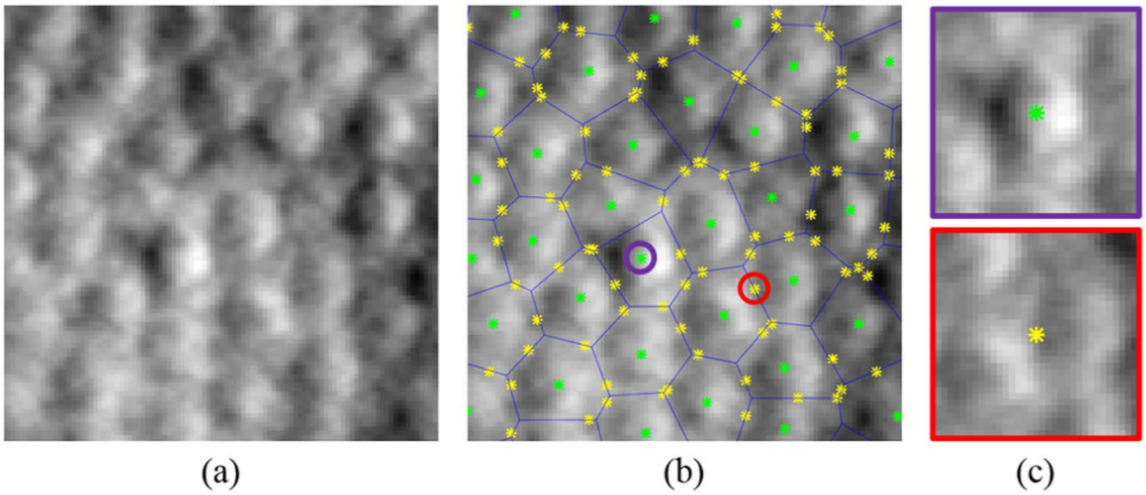


Figure 3. Extraction of labeled patches from cone images. (**a**) Original cropped split detector AOSLO image. (**b**) Image (**a**) with Voronoi diagram overlain in blue. Manually marked cones are shown in green and randomly generated locations along Voronoi edges in yellow. (**c**) Example cone (top-purple) and non-cone (bottom-red) patches (size 33 × 33 pixels) from positions circled in (**b**) with center marked.

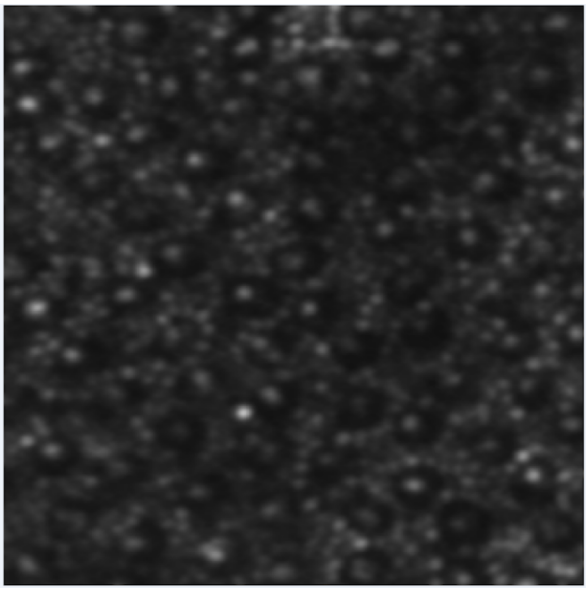
On the other hand, is the Convolutional Neural Network. The work I need to get done is to follow the architecture to build the Neural Network that classifies Cones, Rods, and Backgrounds.

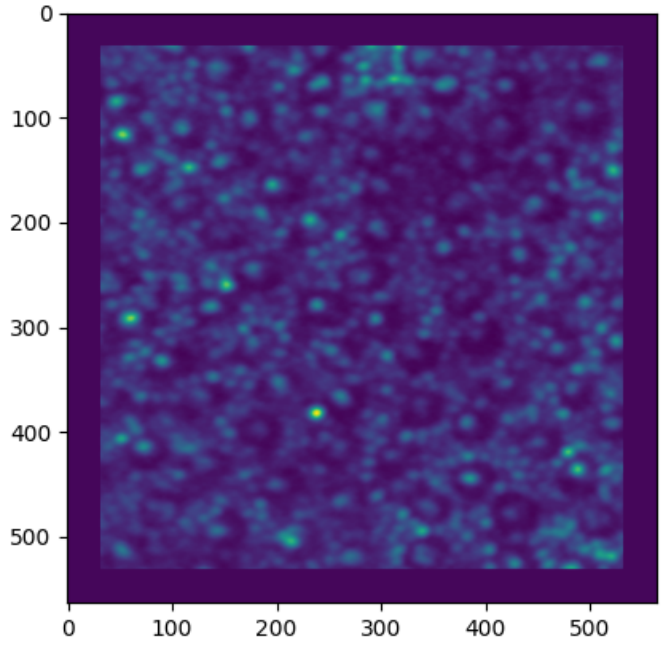
Layer number	Type	Input size	Filter size	Stride	Number of kernels/nodes
1	Convolution	$33 \times 33 \times 1$	$5 \times 5 \times 1$	1	32
2	Batch Normalization	$33 \times 33 \times 32$	—	—	—
3	Max Pooling	$33 \times 33 \times 32$	3×3	2	—
4	ReLU	$16 \times 16 \times 32$	—	—	—
5	Convolution	$16 \times 16 \times 32$	$5 \times 5 \times 32$	1	32
6	Batch Normalization	$16 \times 16 \times 32$	—	—	—
7	ReLU	$16 \times 16 \times 32$	—	—	—
8	Average Pooling	$16 \times 16 \times 32$	3×3	2	—
9	Convolution	$8 \times 8 \times 32$	$5 \times 5 \times 32$	1	64
10	Batch Normalization	$8 \times 8 \times 64$	—	—	—
11	ReLU	$8 \times 8 \times 64$	—	—	—
12	Average Pooling	$8 \times 8 \times 64$	3×3	2	—
13	Fully Connected	$4 \times 4 \times 64$	$4 \times 4 \times 64$	—	64
14	Batch Normalization	$1 \times 1 \times 64$	—	—	—
15	ReLU	$1 \times 1 \times 64$	—	—	—
16	Fully Connected	$1 \times 1 \times 64$	$1 \times 1 \times 64$	—	2
17	Soft-max	$1 \times 1 \times 2$	—	—	—

Table 1. Architecture of the CNN.

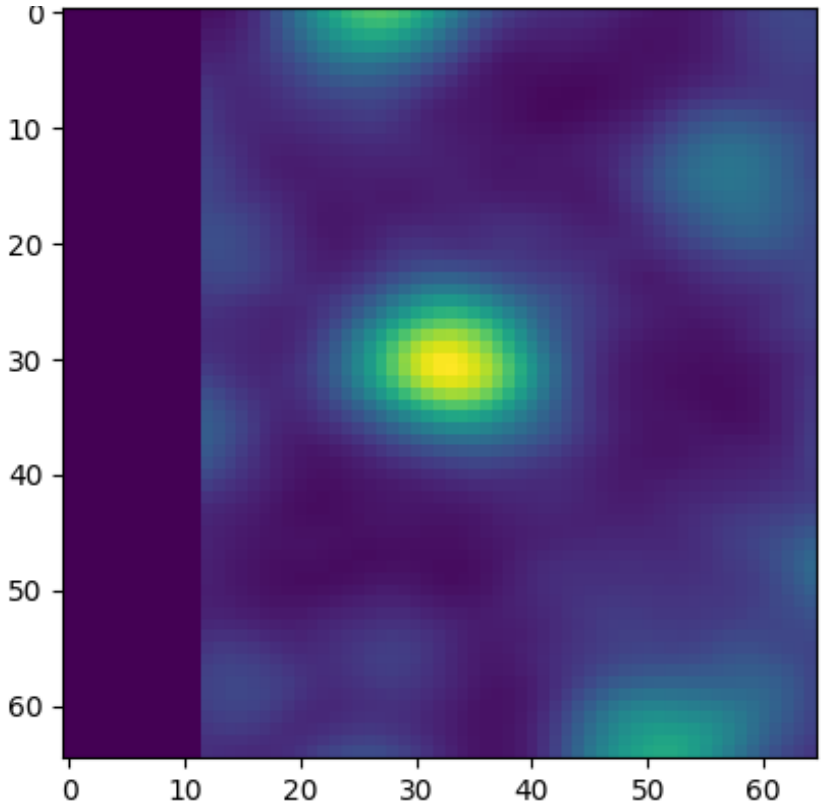
Challenges and Solutions

1. The first challenge I am facing is the sample points on the edges. If a cell sample is located on the edge, it is impossible for the Neural network to learn an incomplete matrix. The solution I choose is to add a dark frame on the edge of each image, so the sample generator can get a complete matrix that can pass into the Neural Network. The following images are the original AO-SLO image and the corresponding image generated from my Solution.



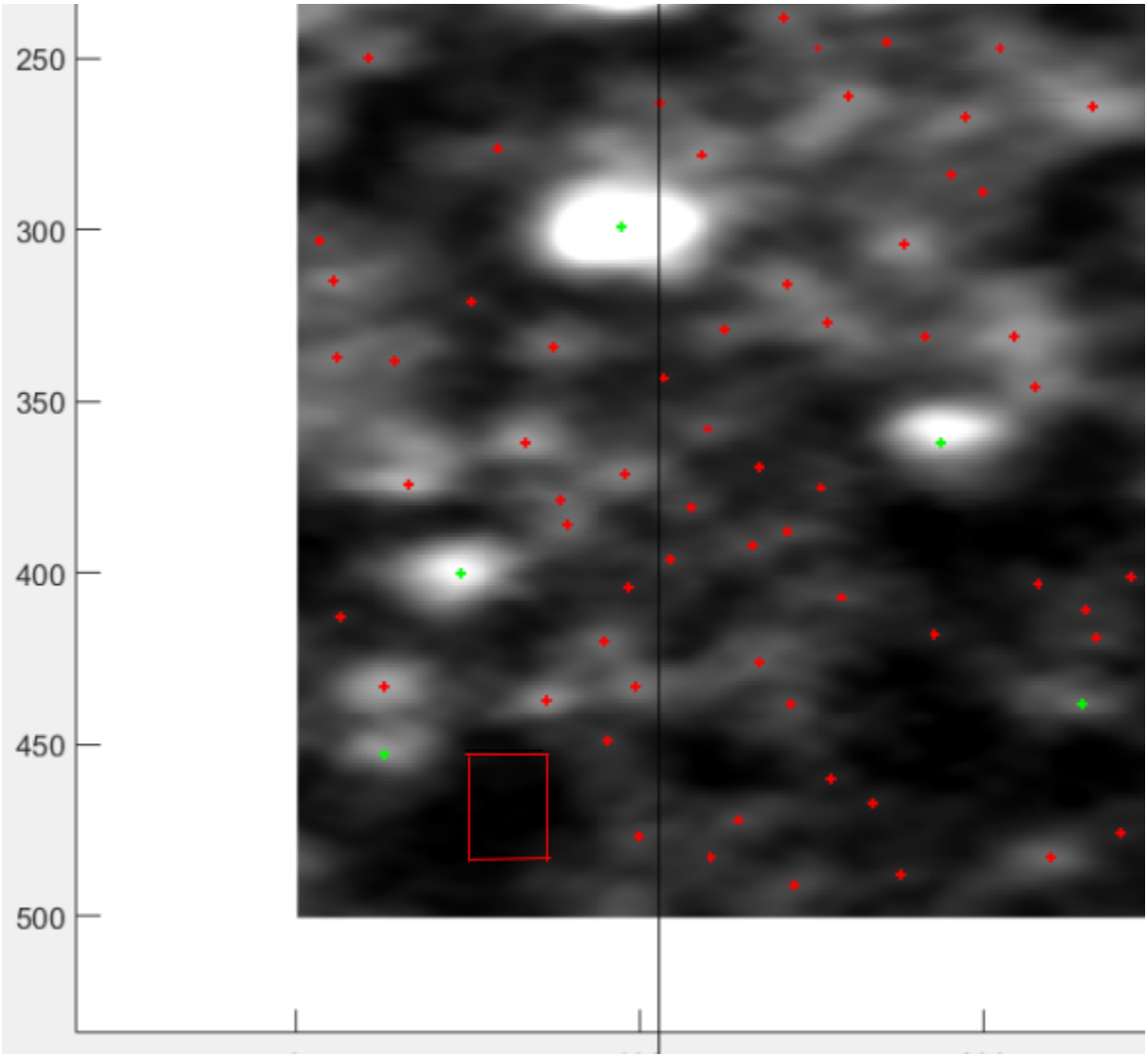


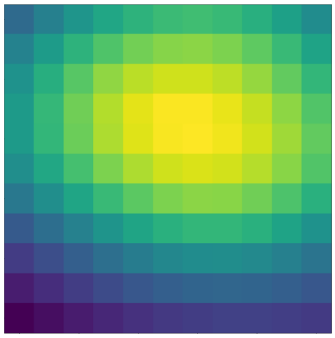
2. The second challenge is the added task on Dr.Cunefare's research. The Neural Network will need to classify the Cones and Rods in different parts of the retina. However, the diameter of the largest cone cells will be more than 30 pixels, which means larger sample patches are needed for the Neural Network to learn all the features of a cone cell. My solution is simple, I pick a larger patch, 65*65, so it will cover all the features of a cell.



3. The third challenge is the black Spots on the image. For example, in the image I showed at the end of this paragraph, The bottom left has a large part that is completely dark. It is possible to be a background part, several rod cells, or maybe a hidden Cones in it. However, it is impossible for us humans to determine. The solution I work out for this challenge is to write an algorithm to check whether the center of each patch is brighter than 5000. If all pixels in the center, which is 11*11 are dimmer than 5000, let's say 4999, the whole sample will be ignored by the sample generator. I provide the center fragment

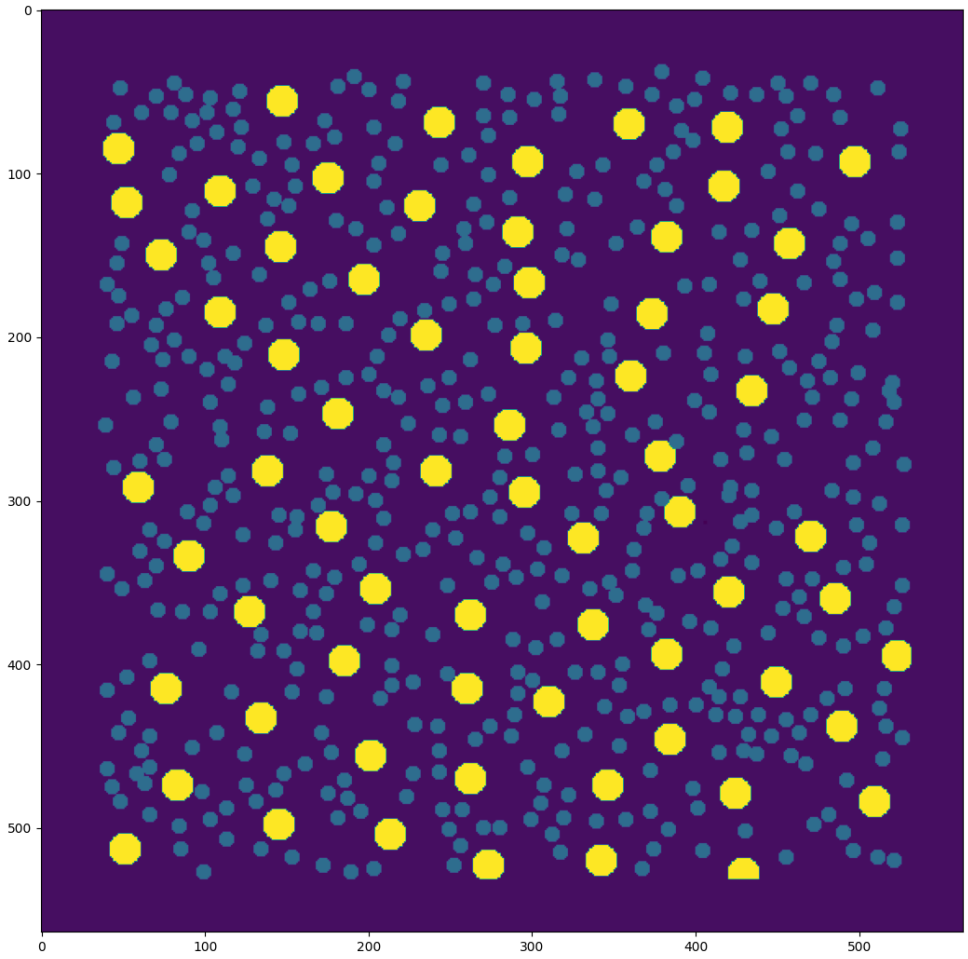
of the upper patch sample.





4. The 4th challenge is the one that holds me the most. In Dr.Cunefare's work, the background sample points are on the Voronoi edges. But, in different parts of the retina, the size ratio between cones and rods is variating, which increases a huge difficulty to generate the Voronoi edges for both cones and rods. This will influence a lot in the

sample selecting section. What I am doing is drawing circles around the points that are marked as a cell, randomly picking the pixels inside of a circle as the center of sample patches, and all the other pixels outside the circle are considered as backgrounds. But here comes another issue. In different parts of the retina, the sizes of cones and rods will vary, which means if I draw a larger circle for cones, images of the Fovea center will all be covered by Cones and left only very few points for backgrounds. If I draw a smaller circle for the cones, the sample points for cone cels will become a lot lesser than the sample points of rods, and the neural network will simply classify all the cell samples as rods to get higher accuracy. This is the challenge I am still facing. This is the figure that converted to the circle mode, I am using the radius of 10 for cones and 5 for rods.



5. Challenge 5 is another sample ratio problem that I need to solve. In the end, I generate 1.1 million cone samples, 0.87 million rod samples, and 8 million backgrounds. If the neural network classifies all samples as backgrounds, it will get more than 80% accuracy. Therefore, I need a magic number for background samples that can generate the most valid neural network. This requires multiply training.

6. It is a concern that I am thinking of in challenge 6. The author uses 33*33 patches as training inputs for the NN. However, my patch size is 65*65, which is 4 times larger than

the author's. Therefore, the same NN architecture may not guarantee a good performance. The way to solve this is to add more layers or do more training.

Validate Hypothesis and Conclusion

- Narrow: Can we build an algorithm by using Cunefare's method?
    - Can not get the Voronoi edges for all cones and rods. Can not use the same sample selection as Cunefare did. However, still have the possibility to create an algorithm to find the Voronoi edges, but will be more complicated since we need to get a way to know the size ratio of cones and rods in different images.
    - The performance of the same architecture is not guaranteed, will need to try more architecture options and trainings.
- Broad: Is it possible to train a Convolutional Neural Network to recognize the Cone cells and the Rod cells in an AO-SLO image?
    - Still have ways to solve the problems I am facing. But that will require much much more time.

Next steps of research

- Keep dealing with the sampling issues
    - Try some magic numbers in picking samples in challenge 5
    - Try some magic numbers for circle radius in challenge 4.
- Build the CNN, use the same Architecture as Cunefare do
    - Also, try more layers on the architecture
    - Compare the accuracy and Validations
- Try other ways to get the Voronoi edges
    - Focus on the diameter ratio between cones and rods

Reference

- Christine A. Curcio, Kenneth R. Sloan, Robert E. Kalina, and Anita E. Hendrickson (1990) Human photoreceptor topography. Departments of Biological Structure (C.A.C., A.E.H.), Ophthalmology (C.A.C., R.E.K., A.E.H.), and Computer Science (K.R.S.), University of Washington, Seattle, Washington 98195, DOI: 10.1002/cne.902920402
- David Cunefare, Leyuan Fang, Robert F. Cooper, Alfredo Dubra, Joseph Carroll & Sina Farsiu, 26 July 2017. Open source software for automatic detection of cone photoreceptors in adaptive optics ophthalmoscopy using convolutional neural networks. Nature. DOI:10.1038/s41598-017-07103-0