

A Computational Model of Choroideremia

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Financial Disclosures

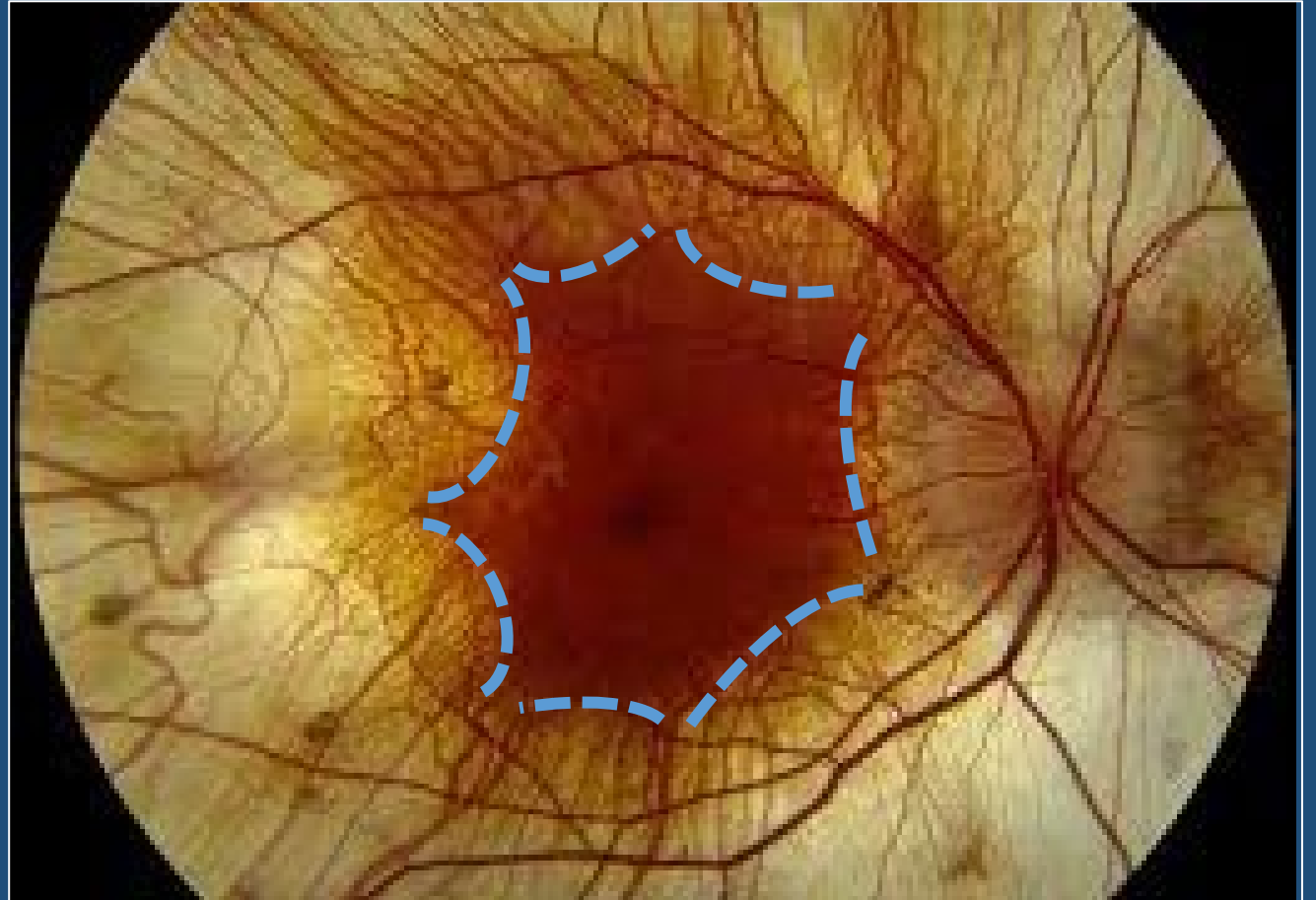
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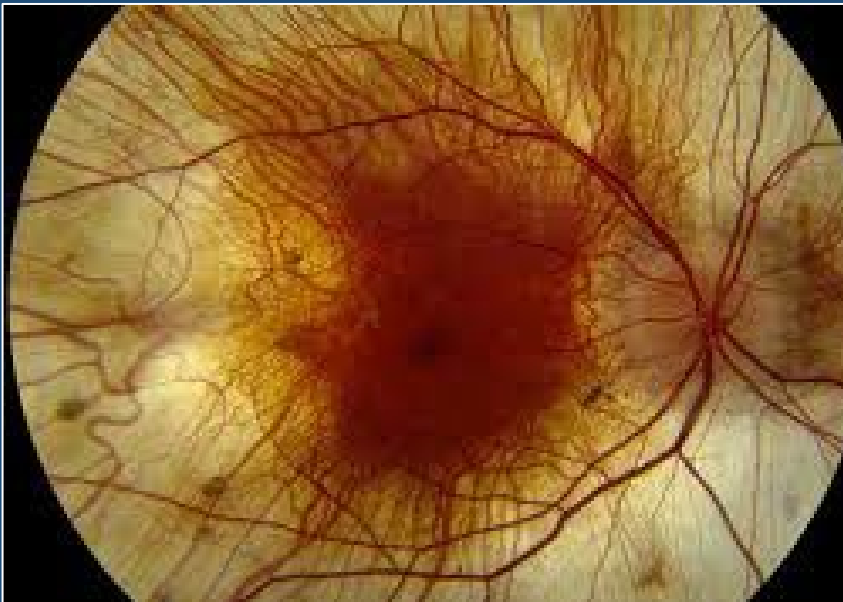
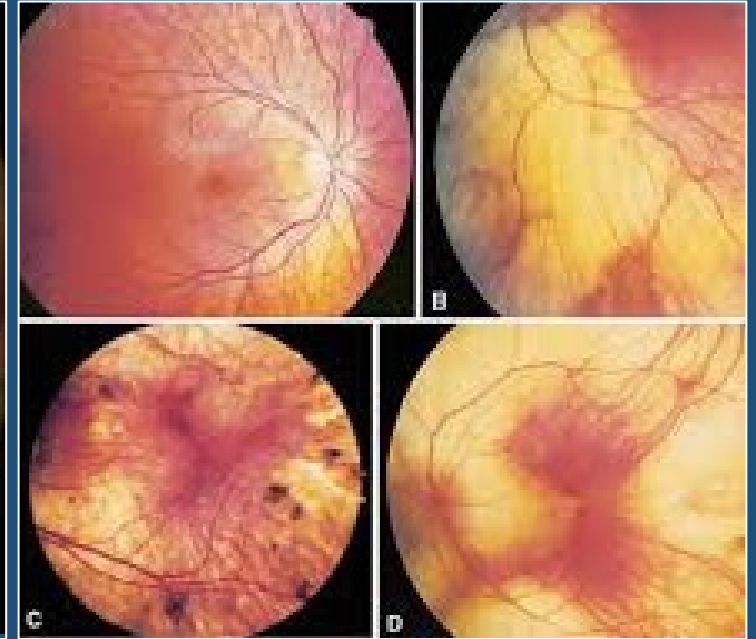
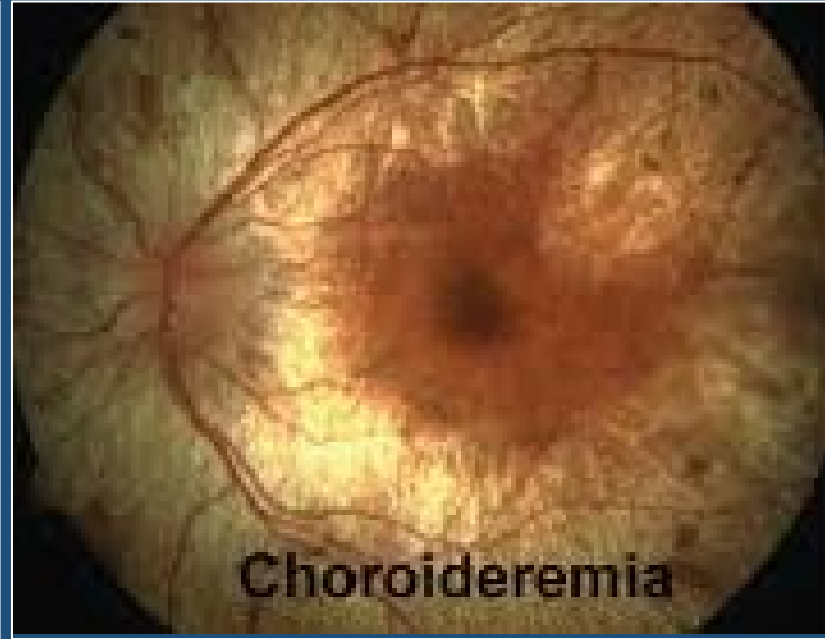
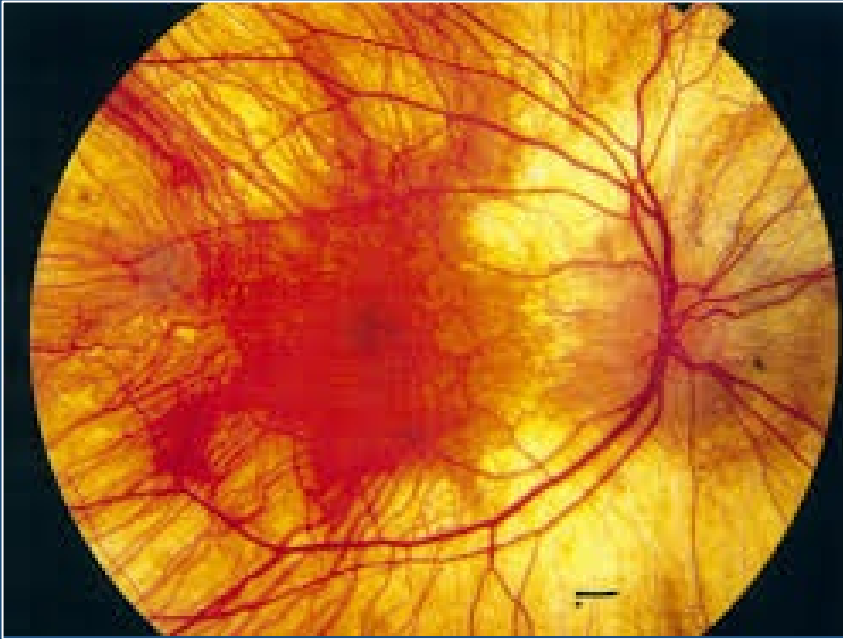
My Role In This Research

- Conception/design of the project
- Acquisition of data
- Analysis and interpretation of data
- Creation and critical review of the presentation

Choroideremia

- Rare, inherited, irreversible, progressive retinal degeneration
- No proven treatment
- No direct animal model
- Characterized by scalloped residual retinal pigment epithelium (RPE)



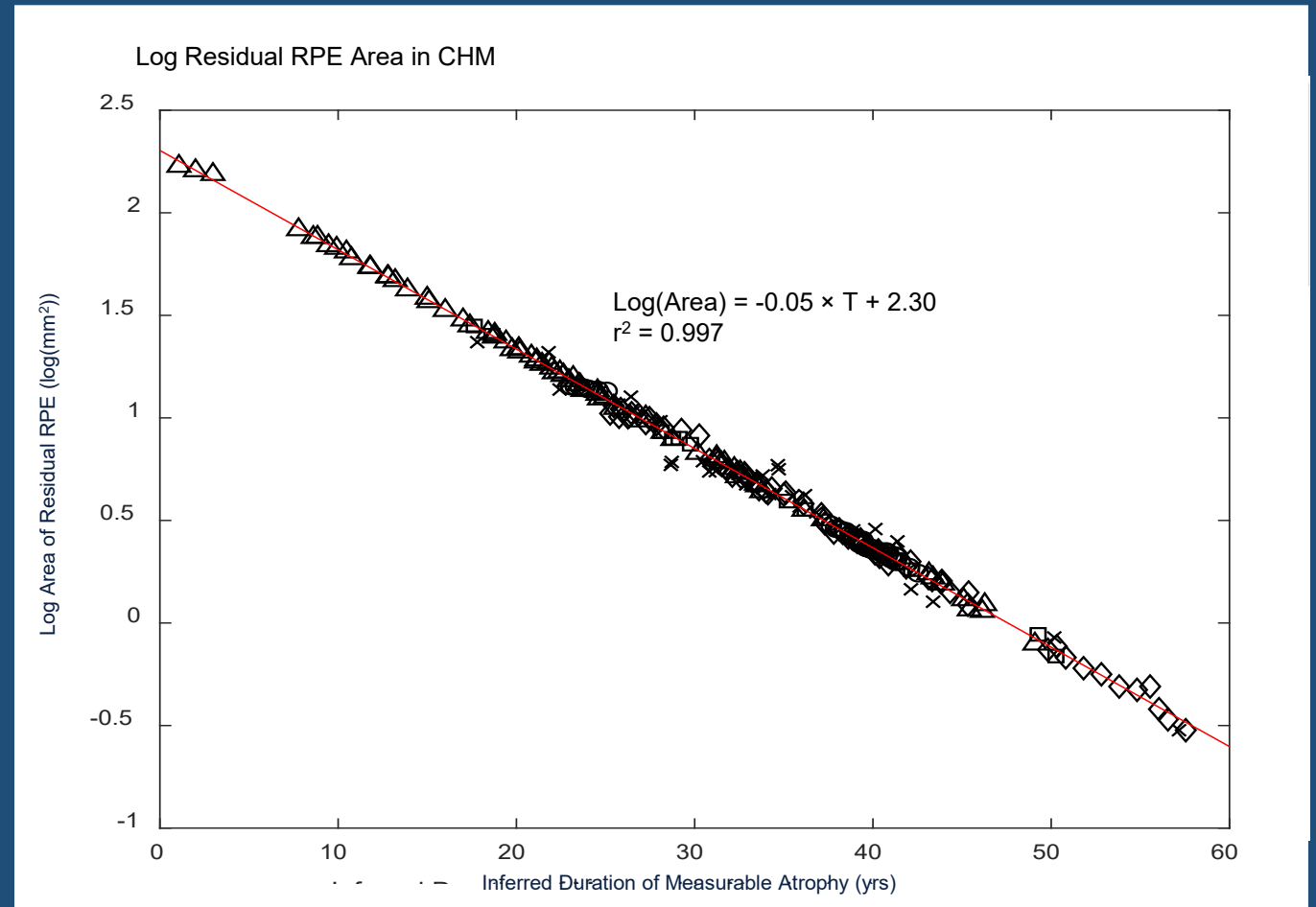


Choroideremia

Why does it have this pattern?

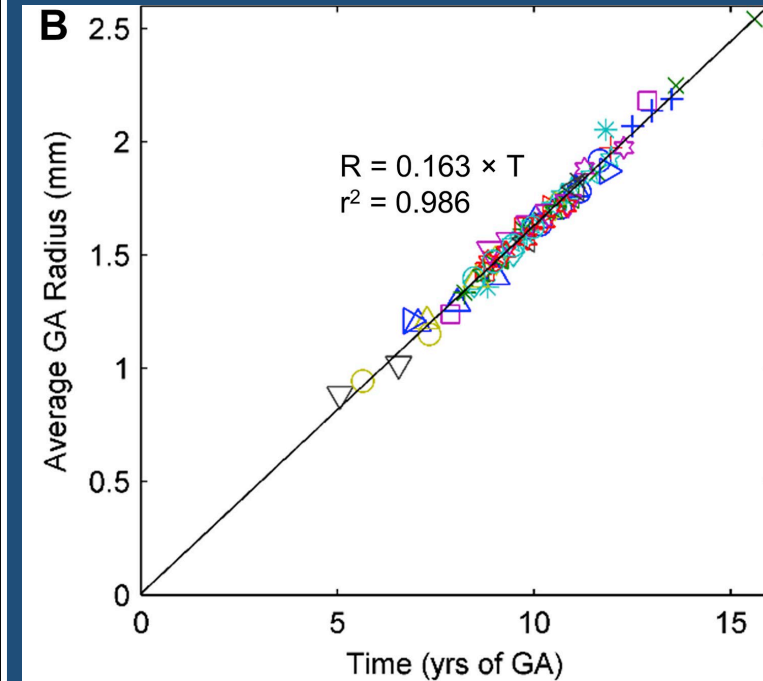
Atrophy Progression in Choroideremia

- After entry time realignment, the Log transformed RPE area declines linearly with time; i.e. **RPE atrophy decays exponentially**



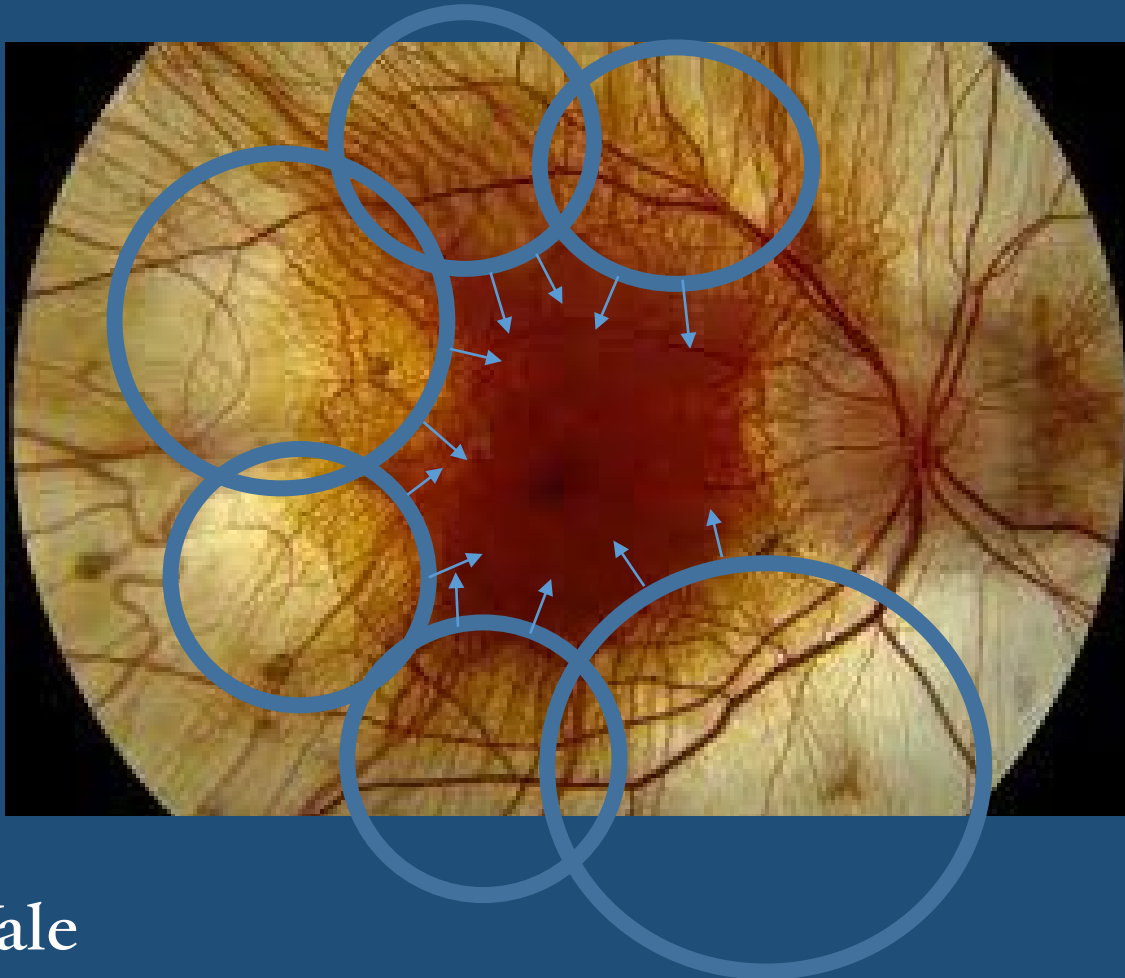
Atrophy Progression in Macular Diseases

- After time entry realignment **RPE atrophy increases linearly with effective radius** in Age-related Macular Degeneration (AMD)



Hypothesis

Can the exponential decay of choroideremia be modeled simply as peripheral atrophy ie a “peripheral AMD”?



- No.
- Does not show exponential decay
- Does not simulate complex scalloped patterns



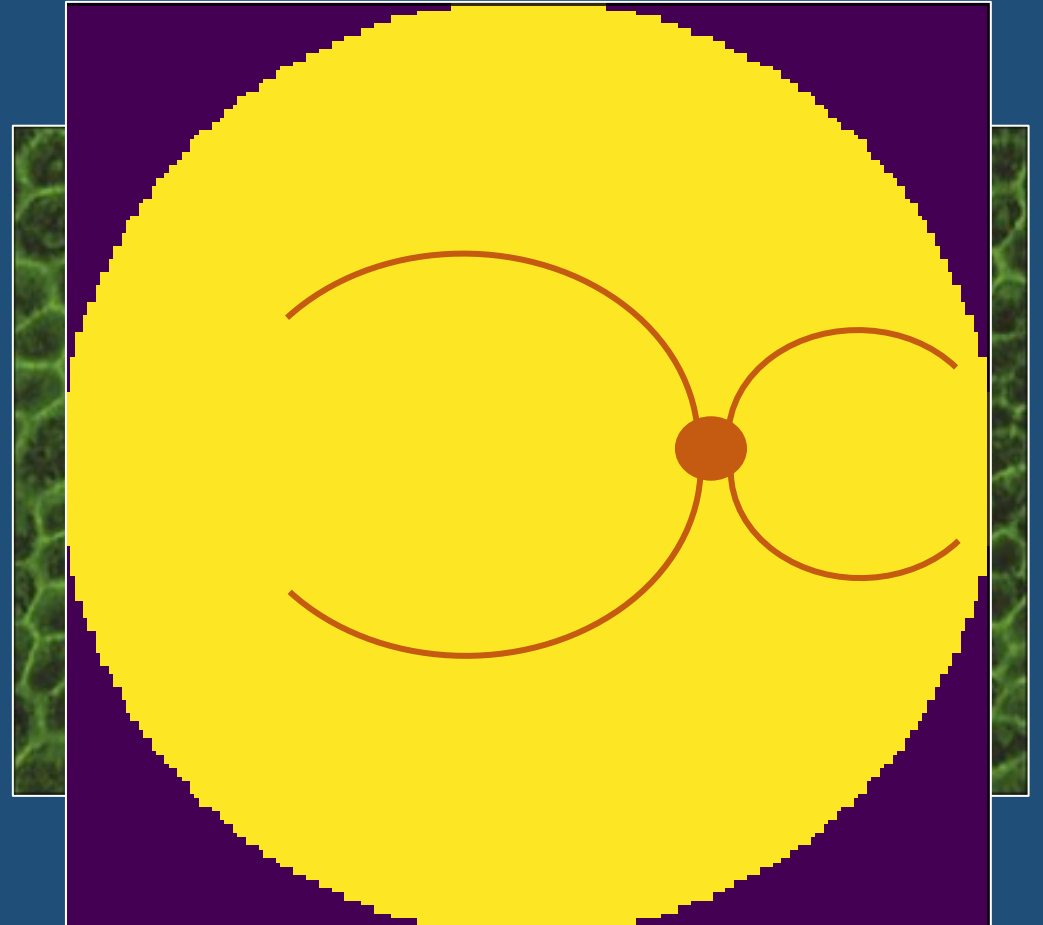


Simply expanding perimeter does
not preserve topography

Inflating a fish does not just make a larger fish

Methods

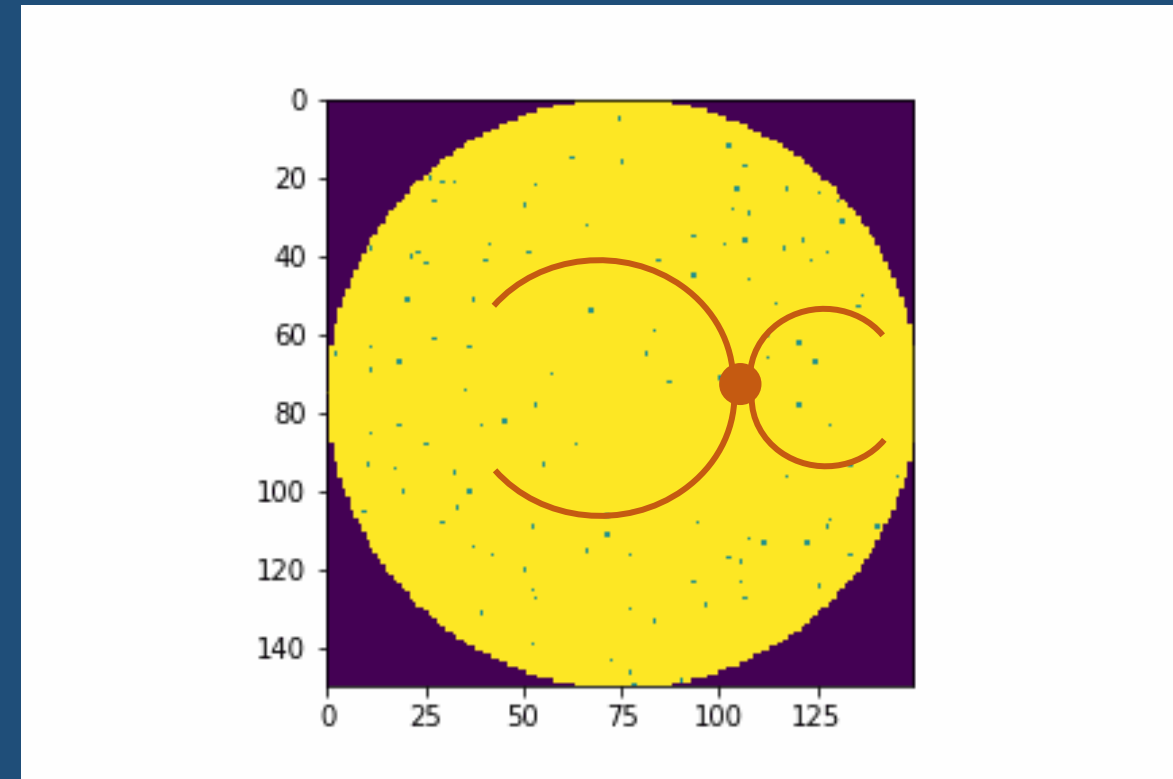
- Developed a simulated model monolayer cell lattice in Python 3.7
 - 1 pixel = 1 cell
 - Yellow = Alive
 - Blue = Atrophied
 - Red = Schematic vessels (not simulated)
 - Purple = Border



Possible Inferences of Choroideremia

1) Background effect: There is a background probability of RPE atrophy defined by an anatomic function

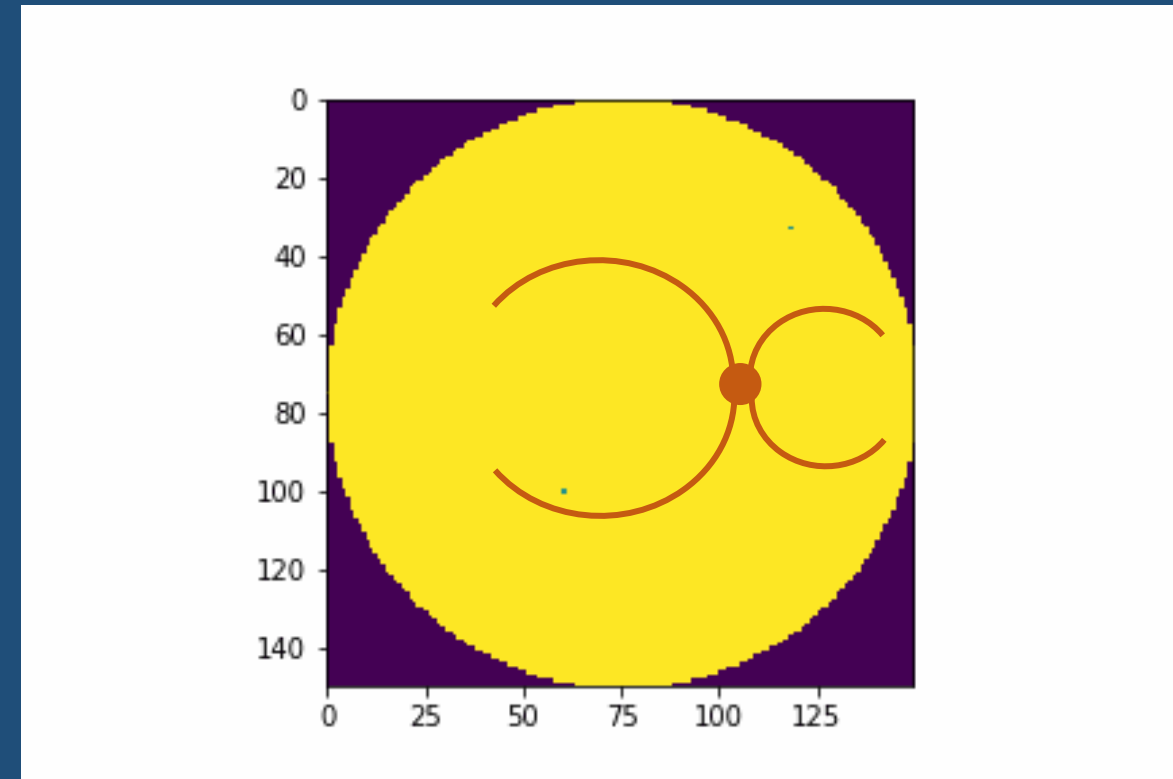
2) Neighbor effect: RPE is interdependent; Neighboring atrophy encourages atrophy



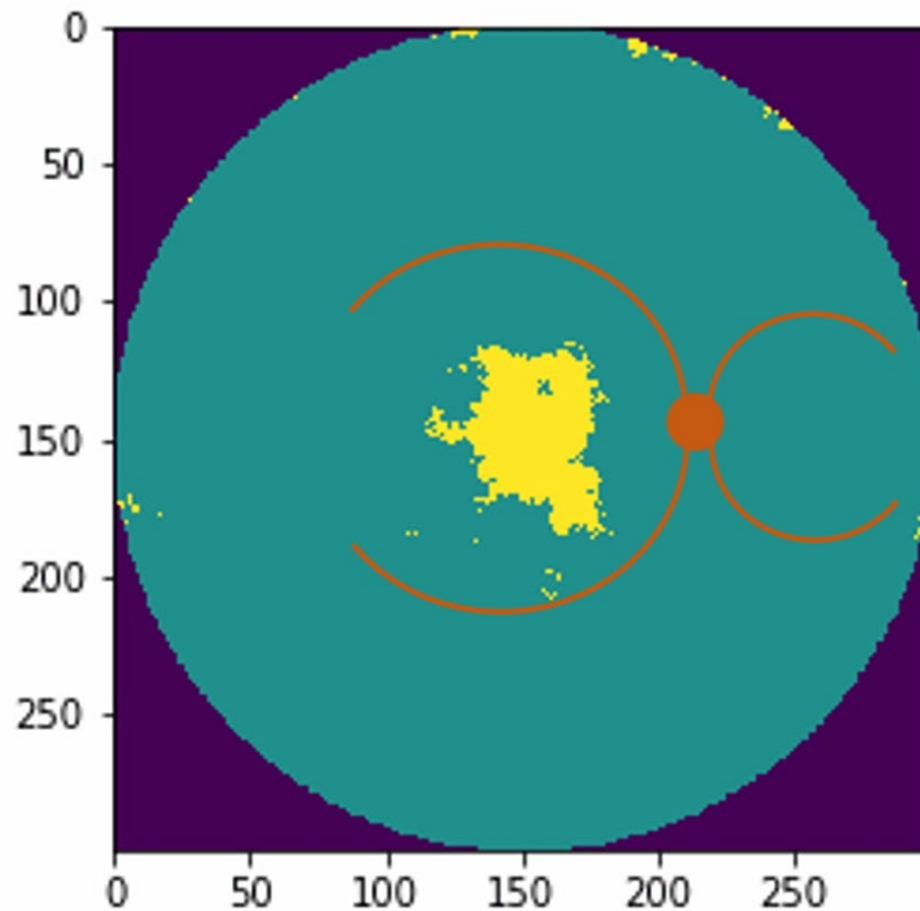
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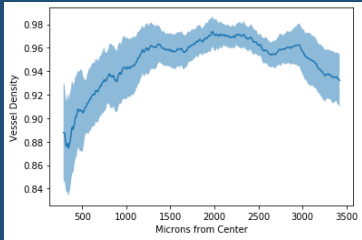
Combining Background and Neighbor Effect



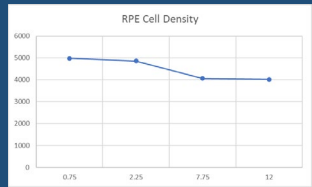
Pathophysiology of Choroideremia

- CHM gene mutation causes dysfunction of vesicular transport protein REP1, which is expressed in:
 - Rods (but not Cones)
 - RPE
 - Choriocapillaris
- Literature conflicts on which layer Choroideremia primarily affects

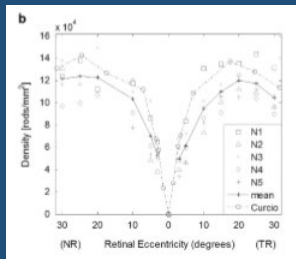
Choriocapillaris Density



RPE Density



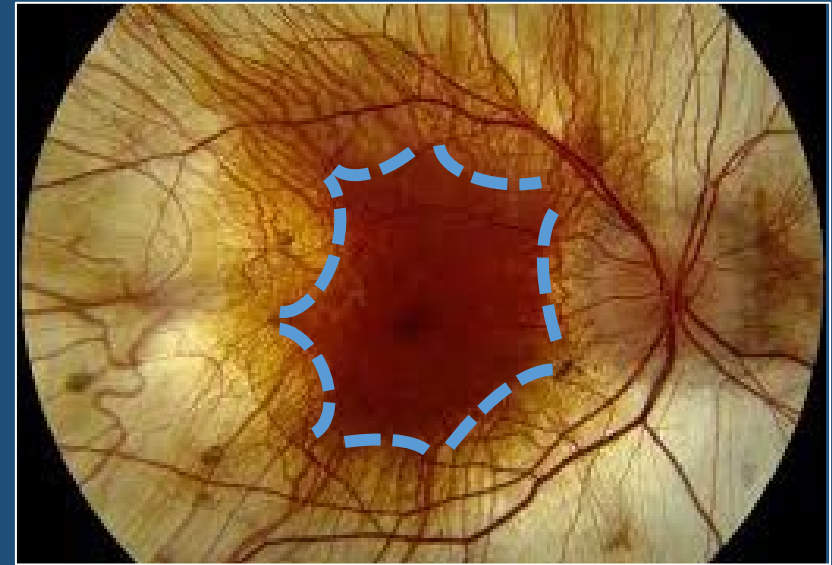
Rod Density



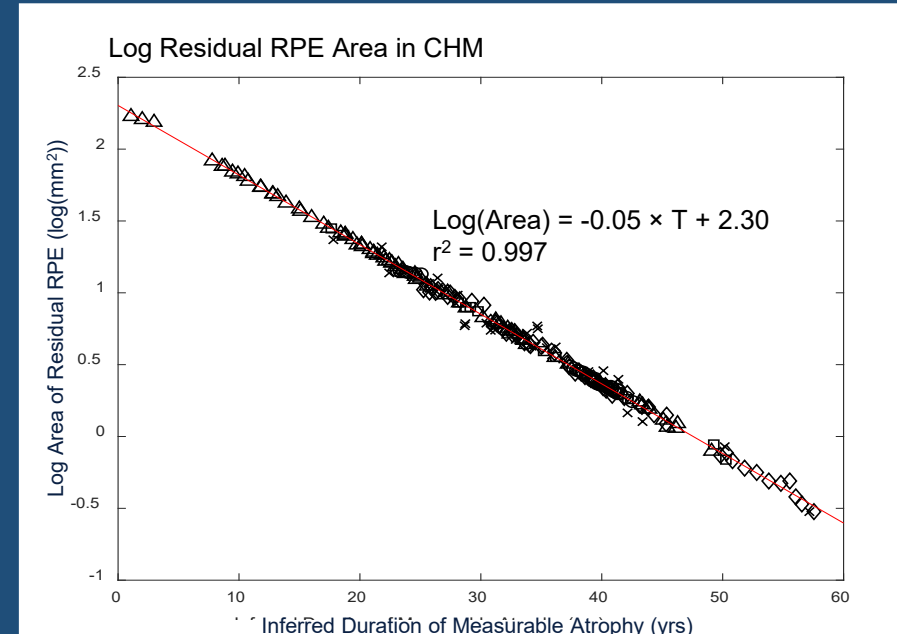
Background Effects Testing Combined with Neighbor Effect



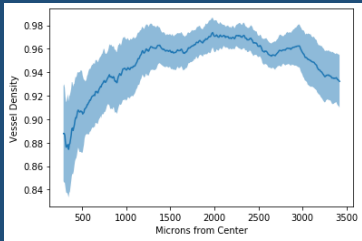
Central Scalloping



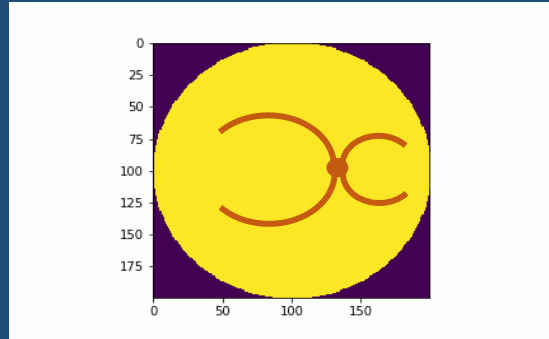
Exponential Decay



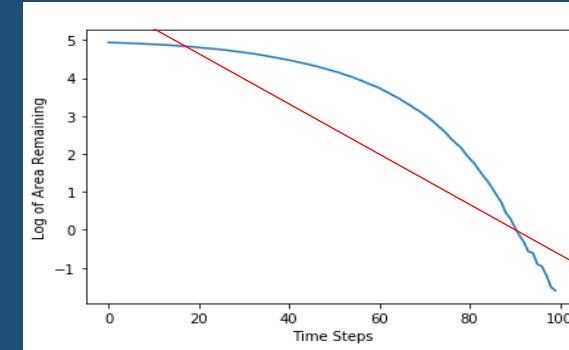
Choriocapillaris Density



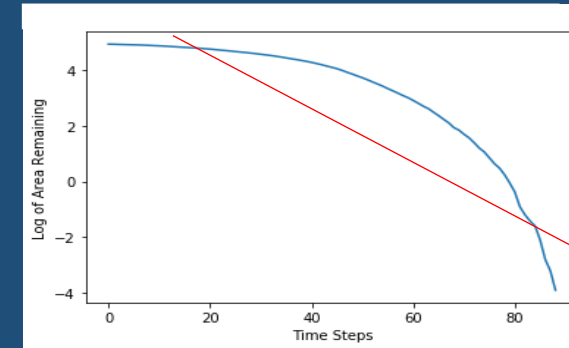
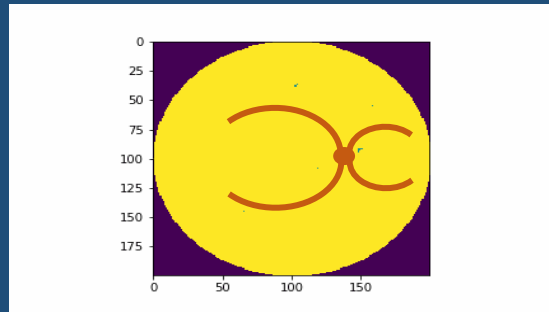
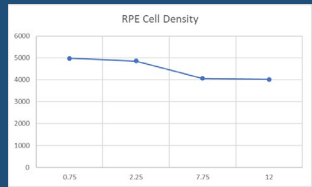
Topography



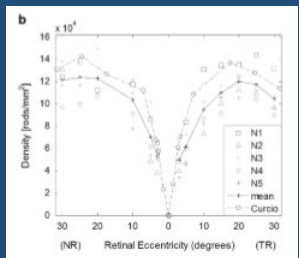
Log Residual Area



RPE Density



Rod Density

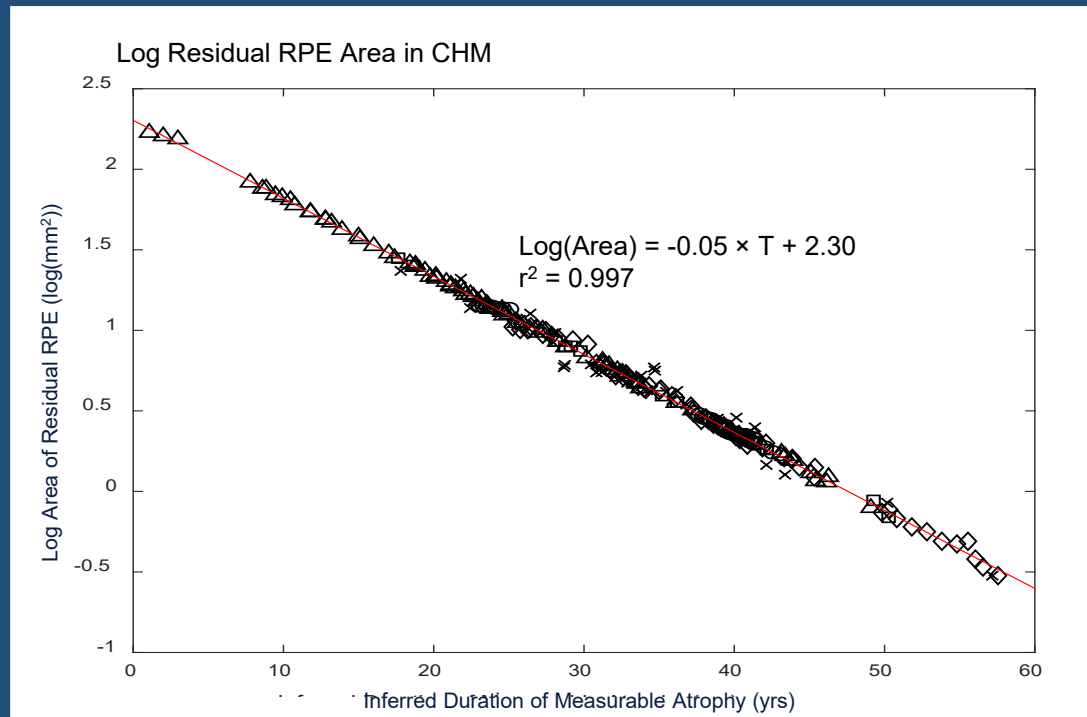


1. Park M, Young BK, Shen LL, Adelman RA, Del Priore LV. Topographic Variation of Retinal and Choroidal Vascular Density in Normal Eyes Using Optical Coherence Tomography Angiography. Manuscript under revision.

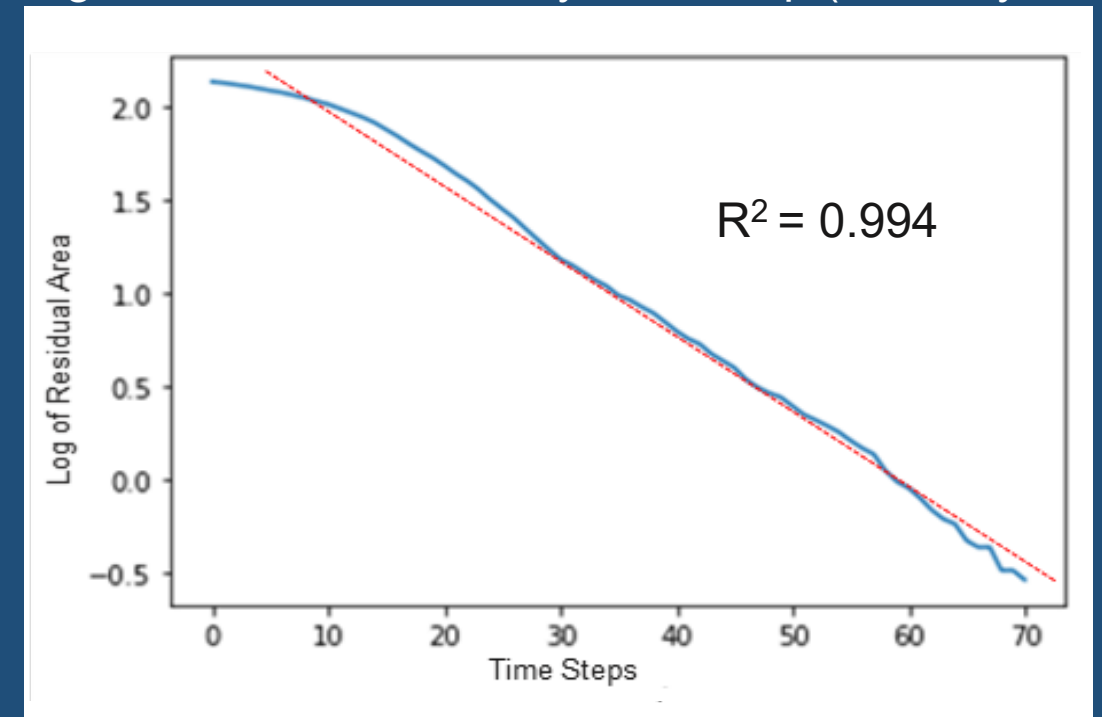
2. Del Priore LV, Kuo Y, Tezel TH; Age-Related Changes in Human RPE Cell Density and Apoptosis Proportion In Situ. *Invest. Ophthalmol. Vis. Sci.* 2002;43(10):3312-3318.

Rod Model Shows Exponential Decay

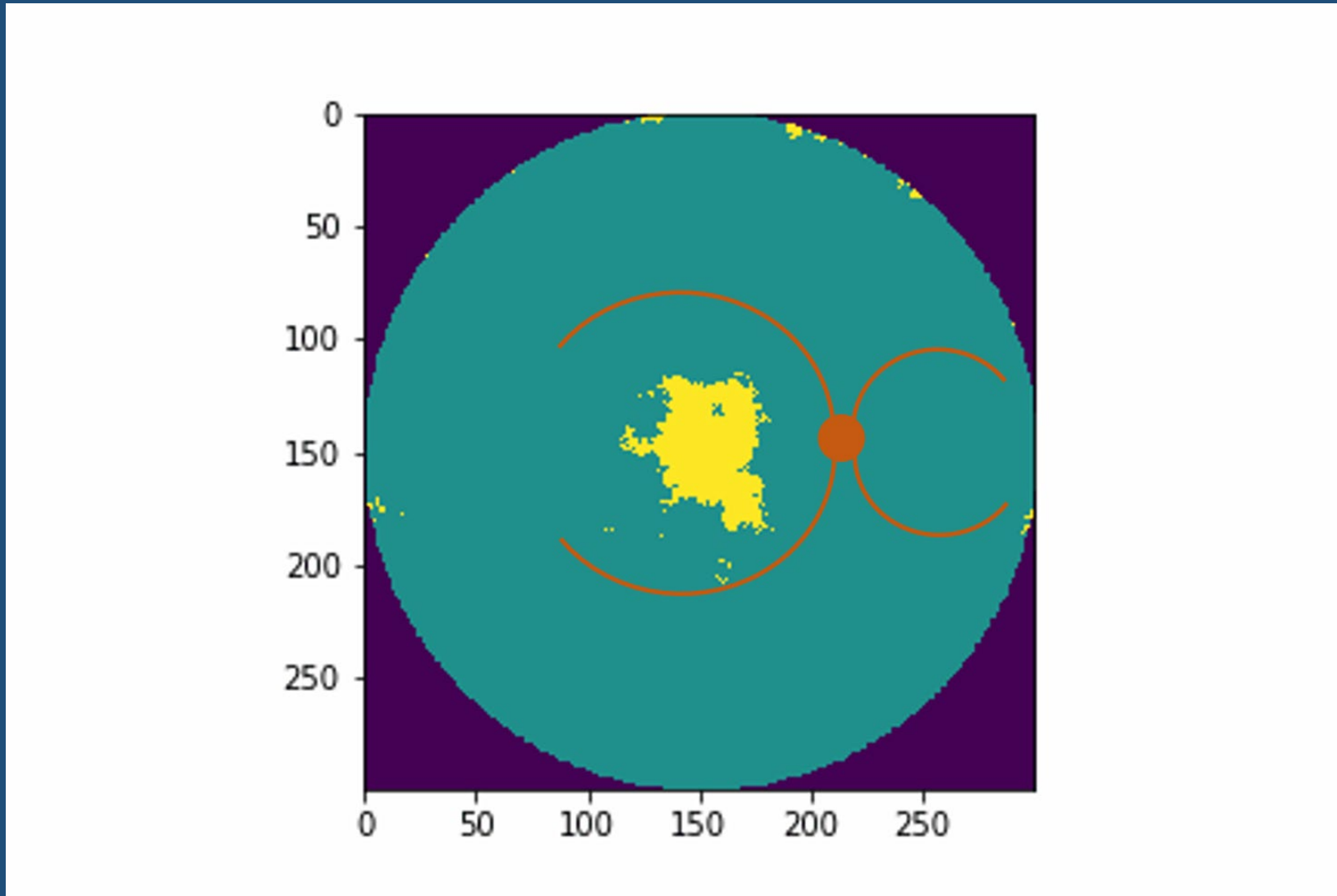
Area Residual RPE by Time Step (Arbitrary Units)



Log Area Residual RPE by Time Step (Arbitrary Units)



Combining Background and Neighbor Effect





Oishi, A., Miyata, M., Numa, S. *et al.* Wide-field fundus autofluorescence imaging in patients with hereditary retinal degeneration: a literature review. *Int J Retin Vitr* 5, 23 (2019).

In Silica Model correlates with In Vivo Data

- **Rod density** is most correlated with Choroideremia, compared to Choriocapillaris density and RPE density
- **Background effect alone** does not explain pattern of atrophy
- **Neighbor effect alone** does not explain exponential decay
- **Coupling Background** and **Neighbor** effect CAN explain the patterns of Choroideremia
- Future Steps: Presenting a unified theory for all types of RPE atrophy

Questions?

Thank you to co-authors Linus Shen and Dr. Lucian Del Priore

Thank you to Dr. Michael Park for providing choriocapillaris density data

Is Choroideremia a Rod-Based Disease?

Possibly. Explanations include:

- Rods are expressing defective gene product
- Rods are most dependent on gene expression in adjacent cell layer

