

Breakout Session 4: Track A

RESHAPE: A Machine Learning Software for Cell Morphometry Analysis of Epithelial Monolayers

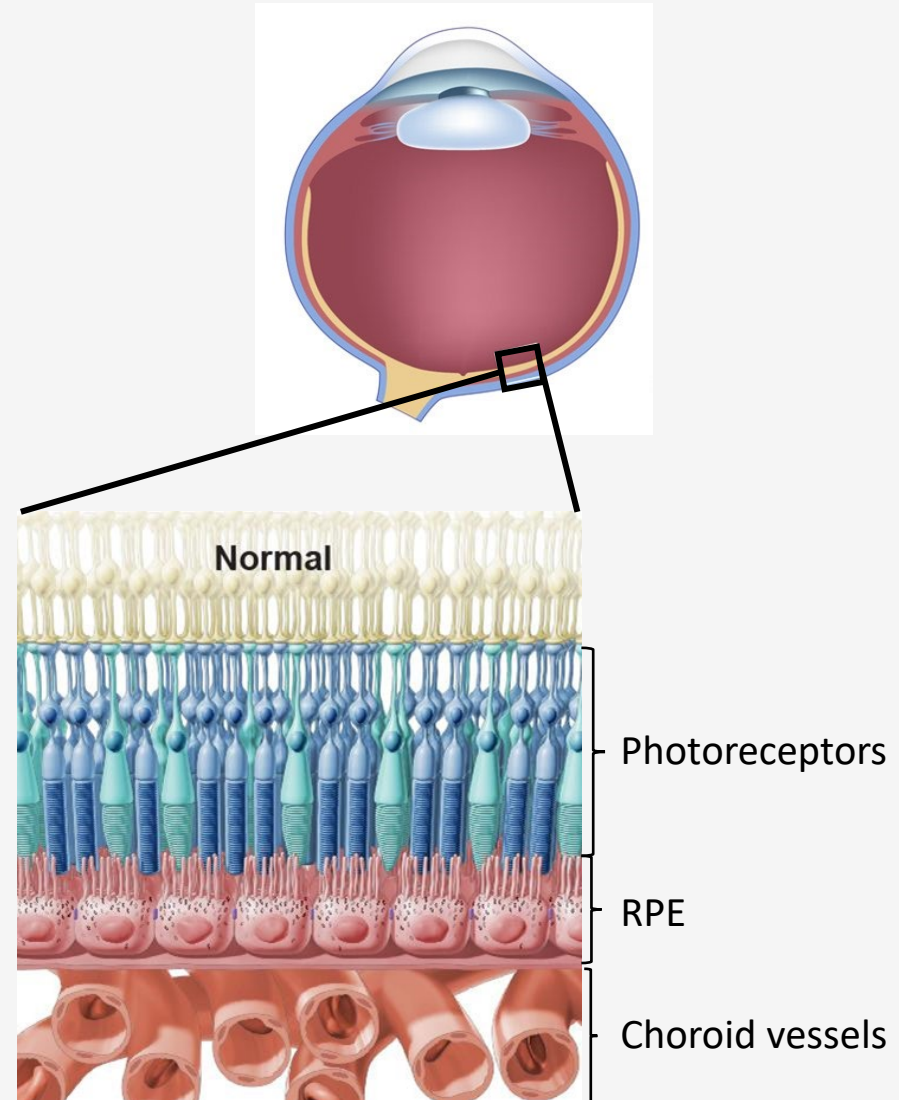
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Postdoc, NEI/NIH

RESHAPE: A Machine Learning Software for Cell Morphometry Analysis of Epithelial Monolayers

Ophthalmic Genetics and Visual Function Branch
National Eye Institute

The Retinal Pigment Epithelium (RPE)

- The Retinal Pigment Epithelium is a monolayer of cells in the back of the eye
- Plays crucial roles in maintaining the normal retinal function and homeostasis.



Regional Retinal Degenerative Diseases

Normal Vision



AMD Vision



RP Vision

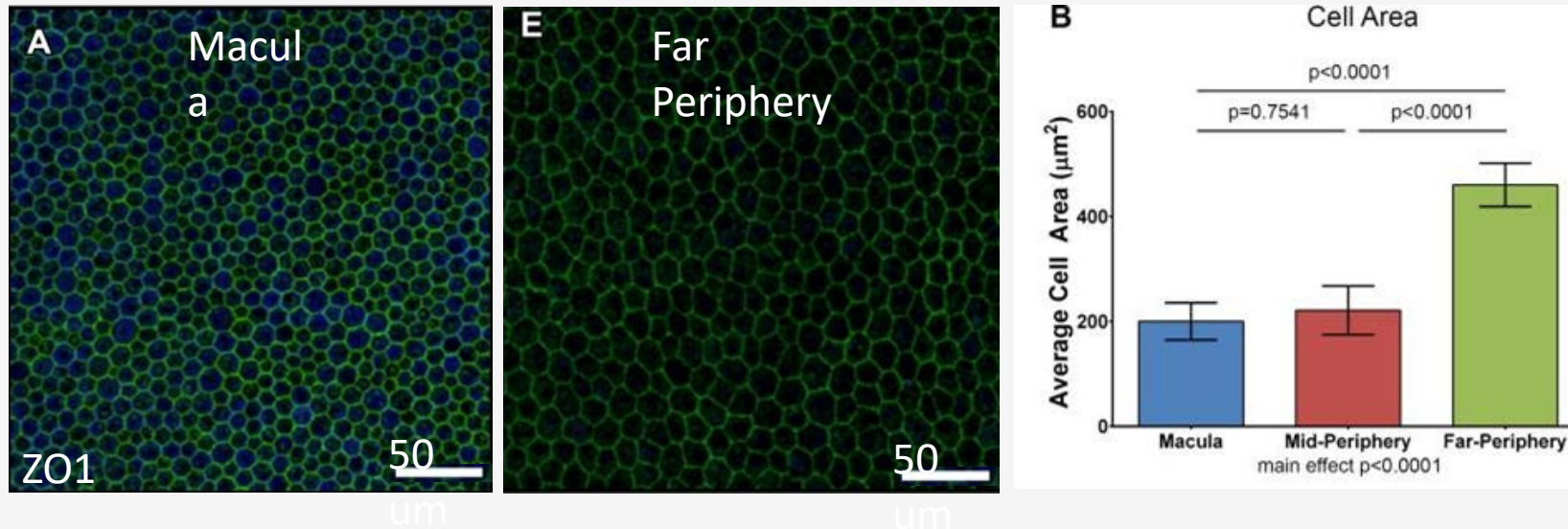


- Macular RPE degeneration leads to Age-related Macular Degeneration (AMD)
- Peripheral RPE defects leads to Retinitis Pigmentosa (RP) (RPE65 mutations)

There are regional RPE differences that underlie different types of regional retinal degeneration.

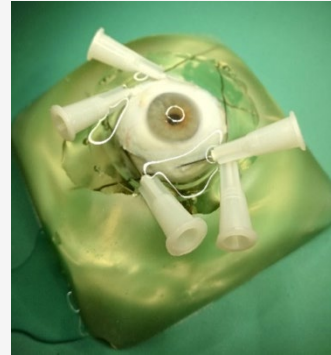
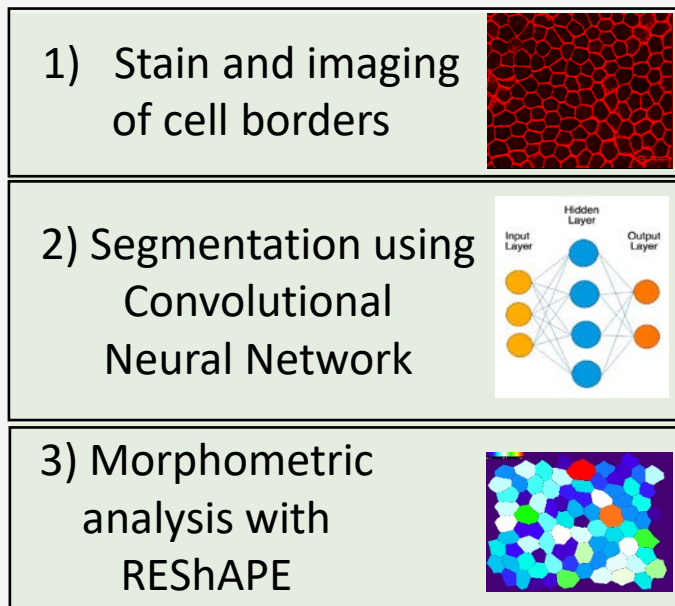
Regional Differences in Retinal Pigment Epithelium (RPE)

Macular RPE cells are smaller than peripheral (Bhatia et al., 2016)



A complete morphometric map of the human RPE monolayer is not currently available

Project Design



Scanning: ~ 200,000 images
~ 17 hours
Img size: 4-7 GB (compressed)

Manual correction
from 11 students

4-5 hours for 3-4 millions cells

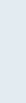


Compare human RPE morphometry

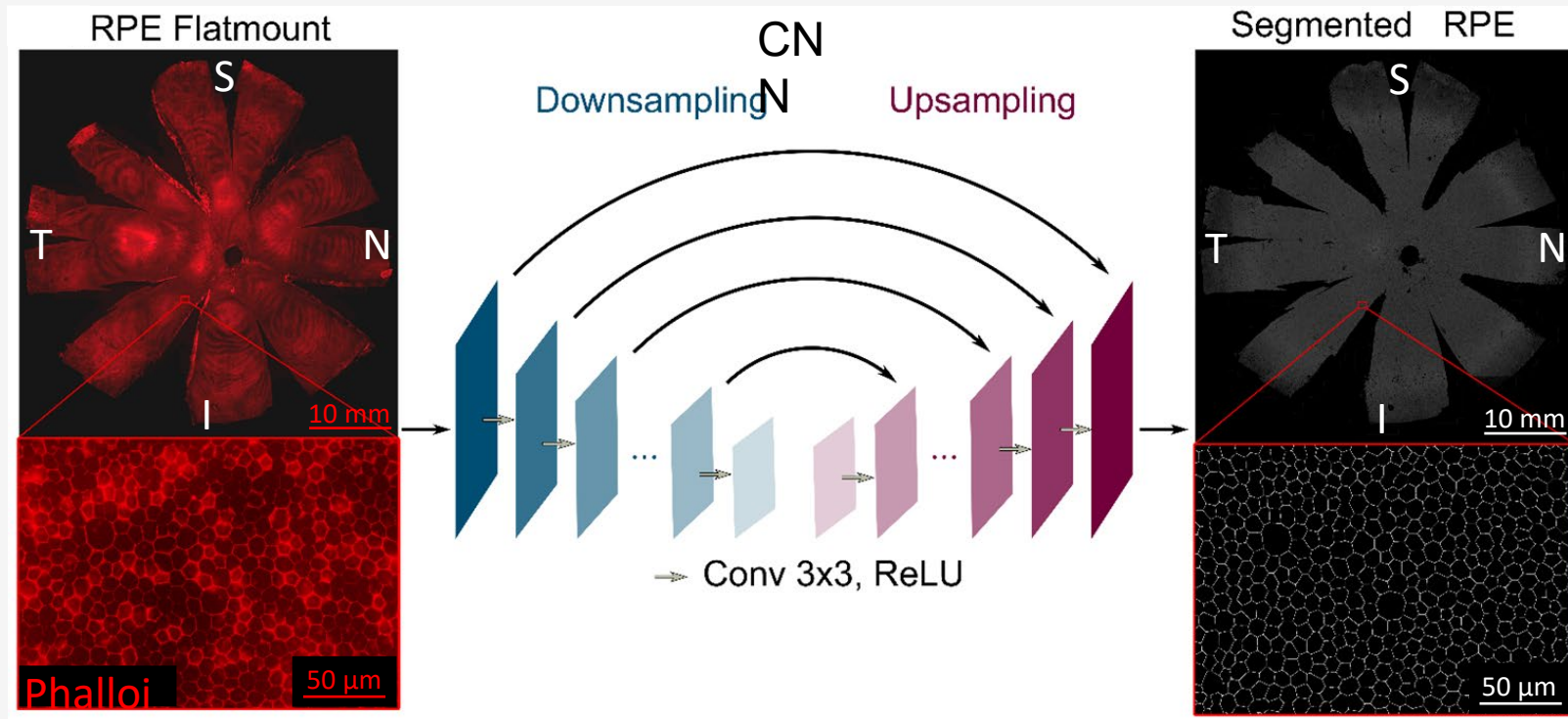
Peripheral RPE



Macular RPE



Segmentation Using Convolutional Neural Network (CNN)



din

S = Superior

N = Nasal

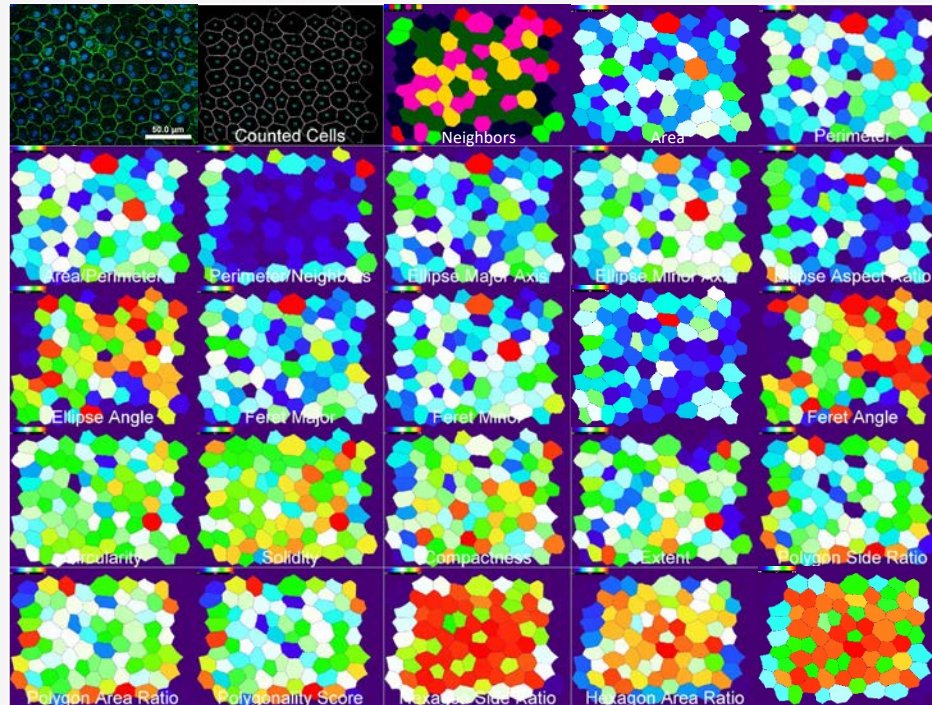
I = Inferior

T = Temporal

Segmentation accuracy 95-98%

Morphometric Analysis with REShAPE

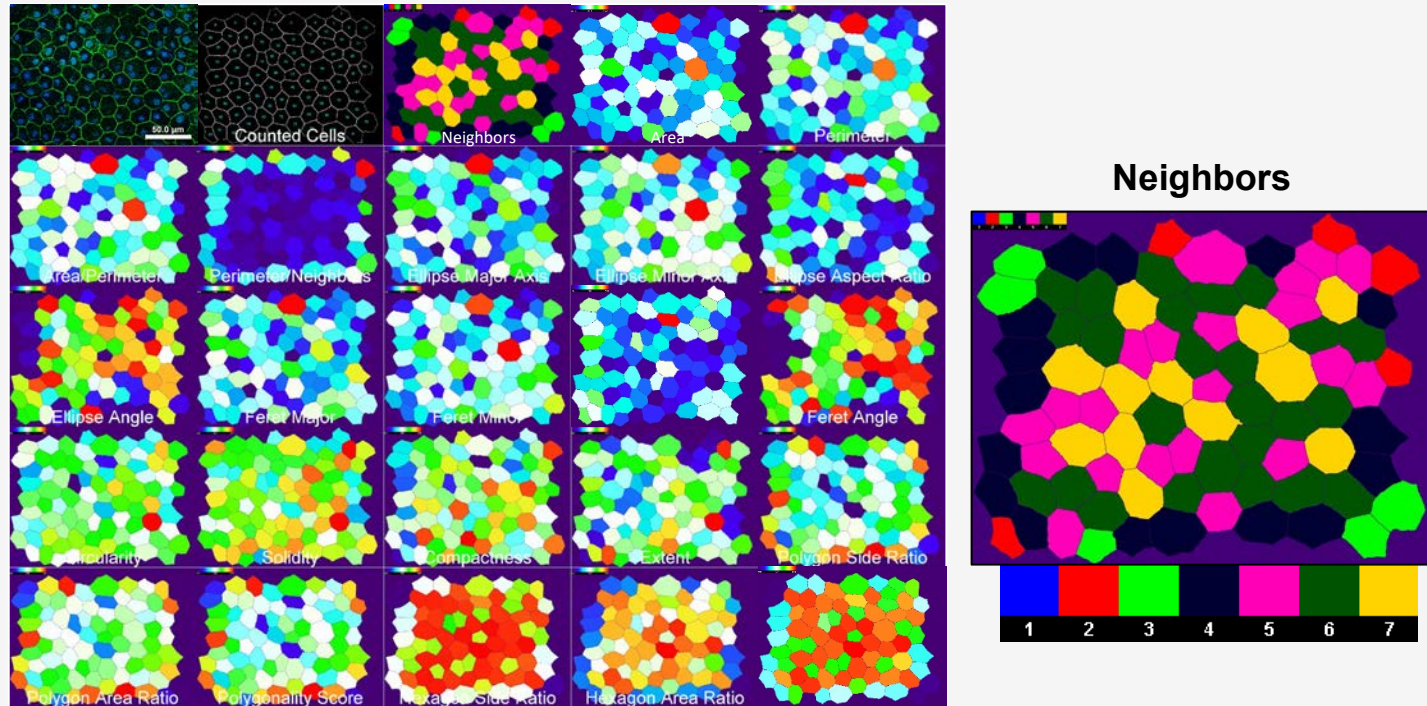
- **Retinal Epithelium Shape And Pigment Evaluator**



- 30 distinct shape metrics
- Creates a graphical montage of cell metrics
- Produces spreadsheet with all raw data for statistical analysis
- Creates summary statistics for all of the metrics
 - Mean, SD, min, max

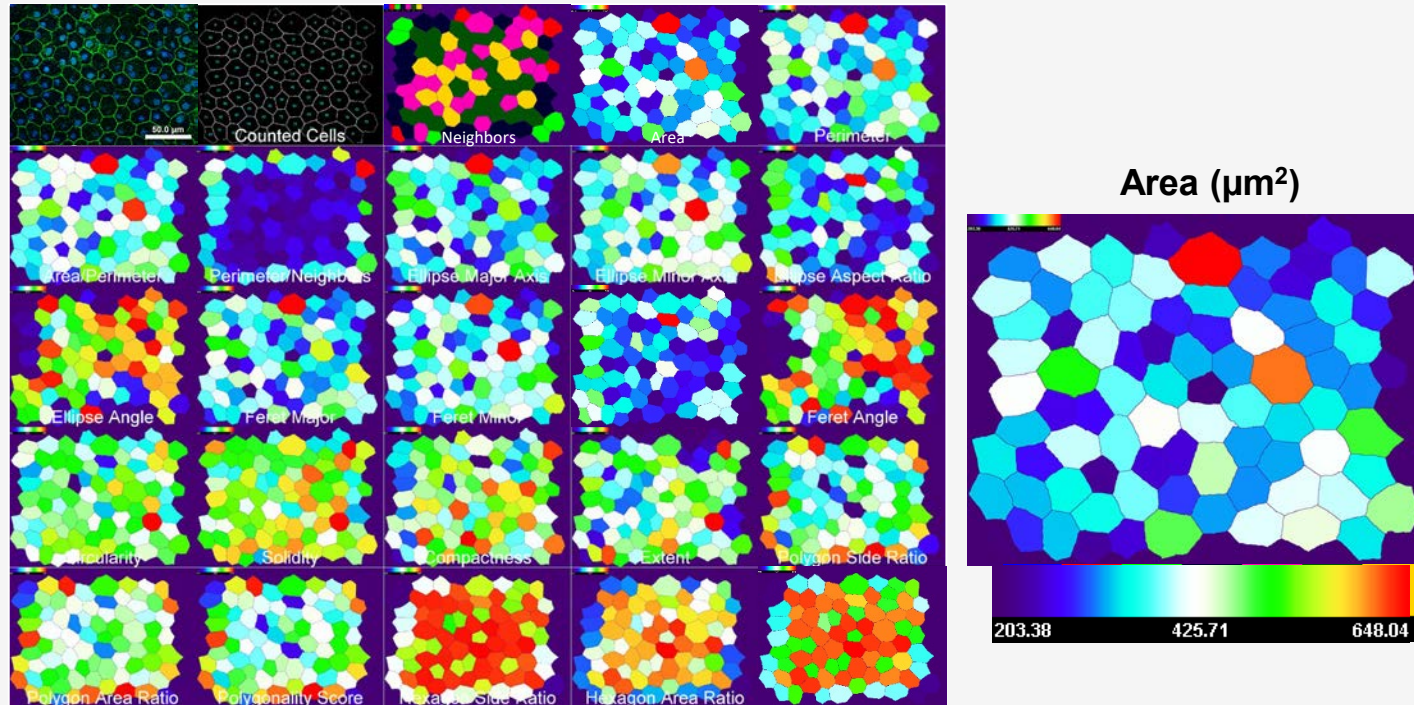
- Schaub and Hotaling et al, *Deep learning predicts function of live retinal pigment epithelium from quantitative microscopy*, Journal of Clinical Investigation, 2020
- Ortolan, D. et al. *Single-cell-resolution map of human retinal pigment epithelium helps discover subpopulations with differential disease sensitivity*. PNAS, 2022

Morphometric Analysis with REShAPE



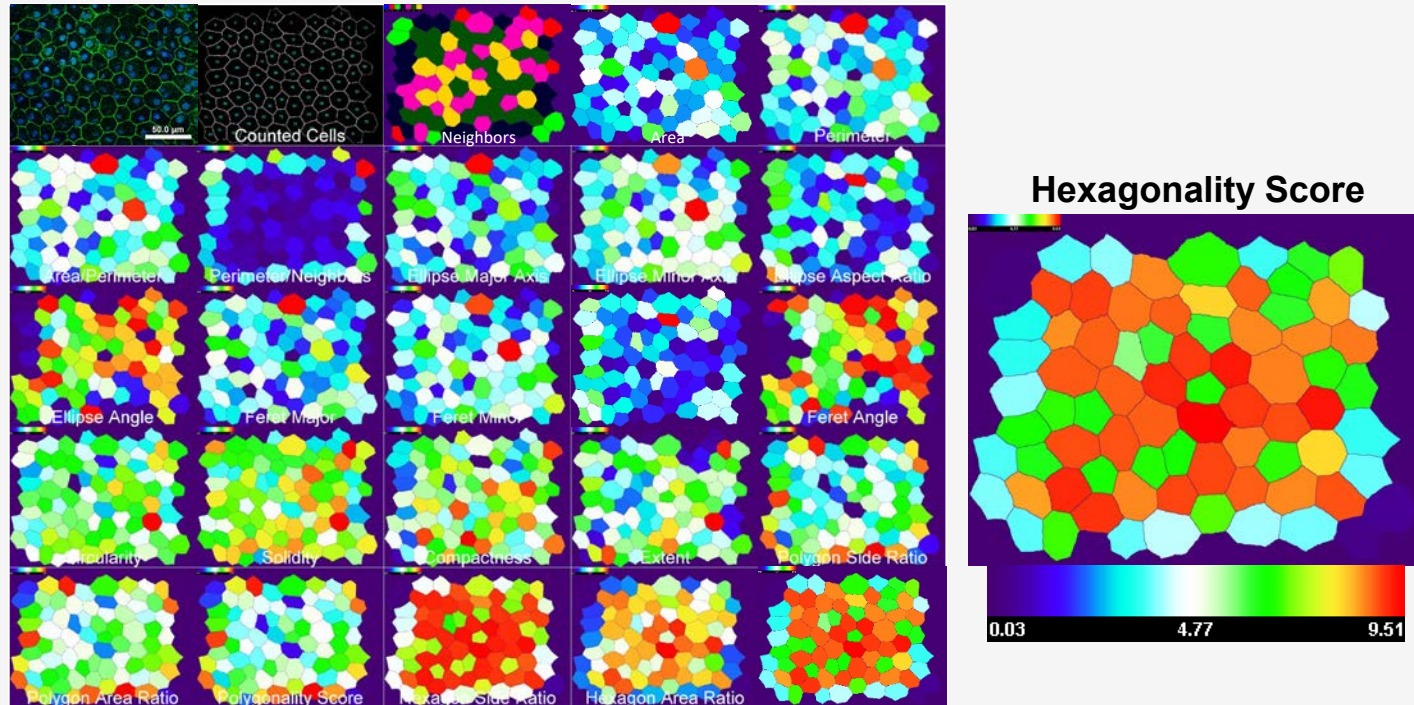
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Morphometric Analysis with REShAPE



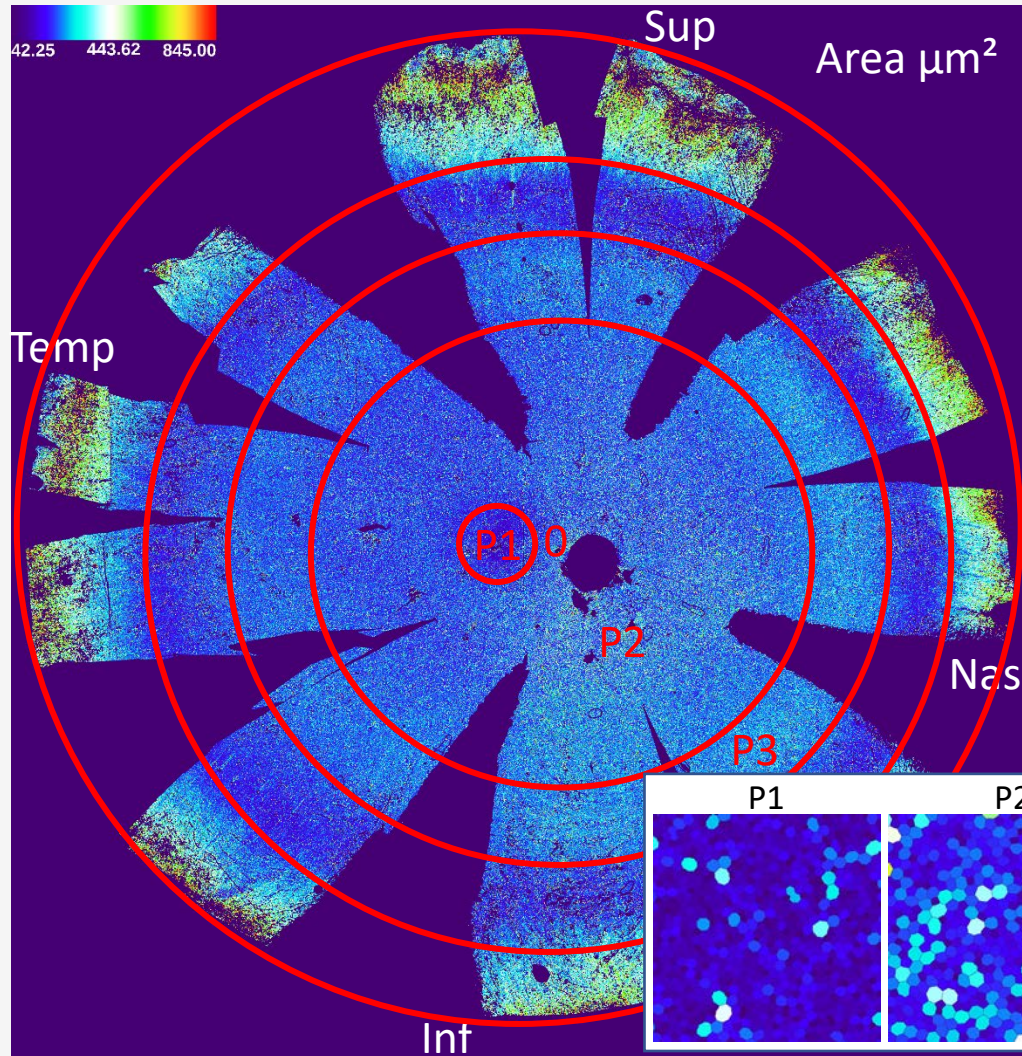
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Morphometric Analysis with REShAPE



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Morphometric Analysis of Human RPE



- Low magnification map of whole human RPE flatmount
- 3-4 millions cells per flatmount
- Every cell is color-coded according to their cell area
- Dark blue = Small area
- Yellow/Red = Big area

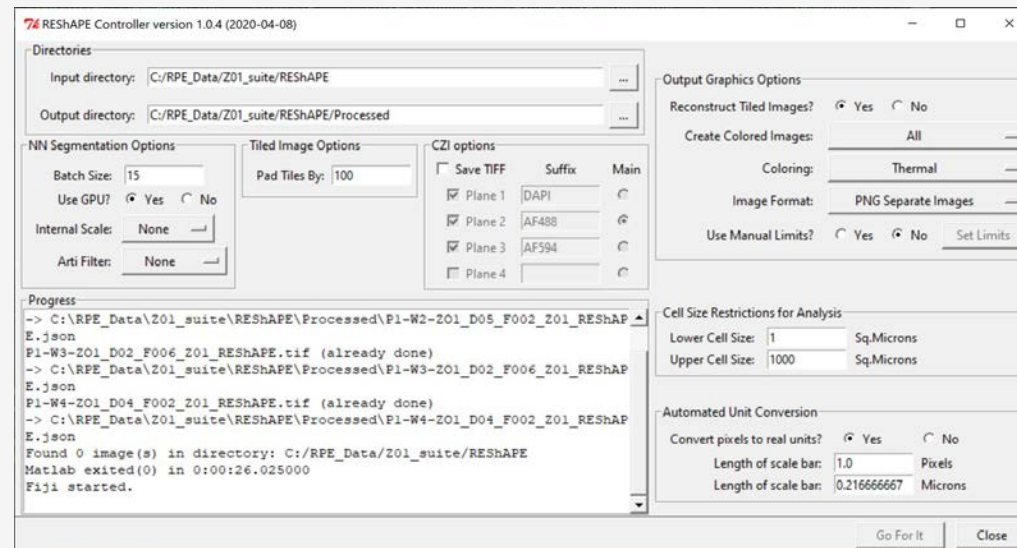
Enhancements and Improvements to REShAPE processing from Strides Initiative

Previous process:

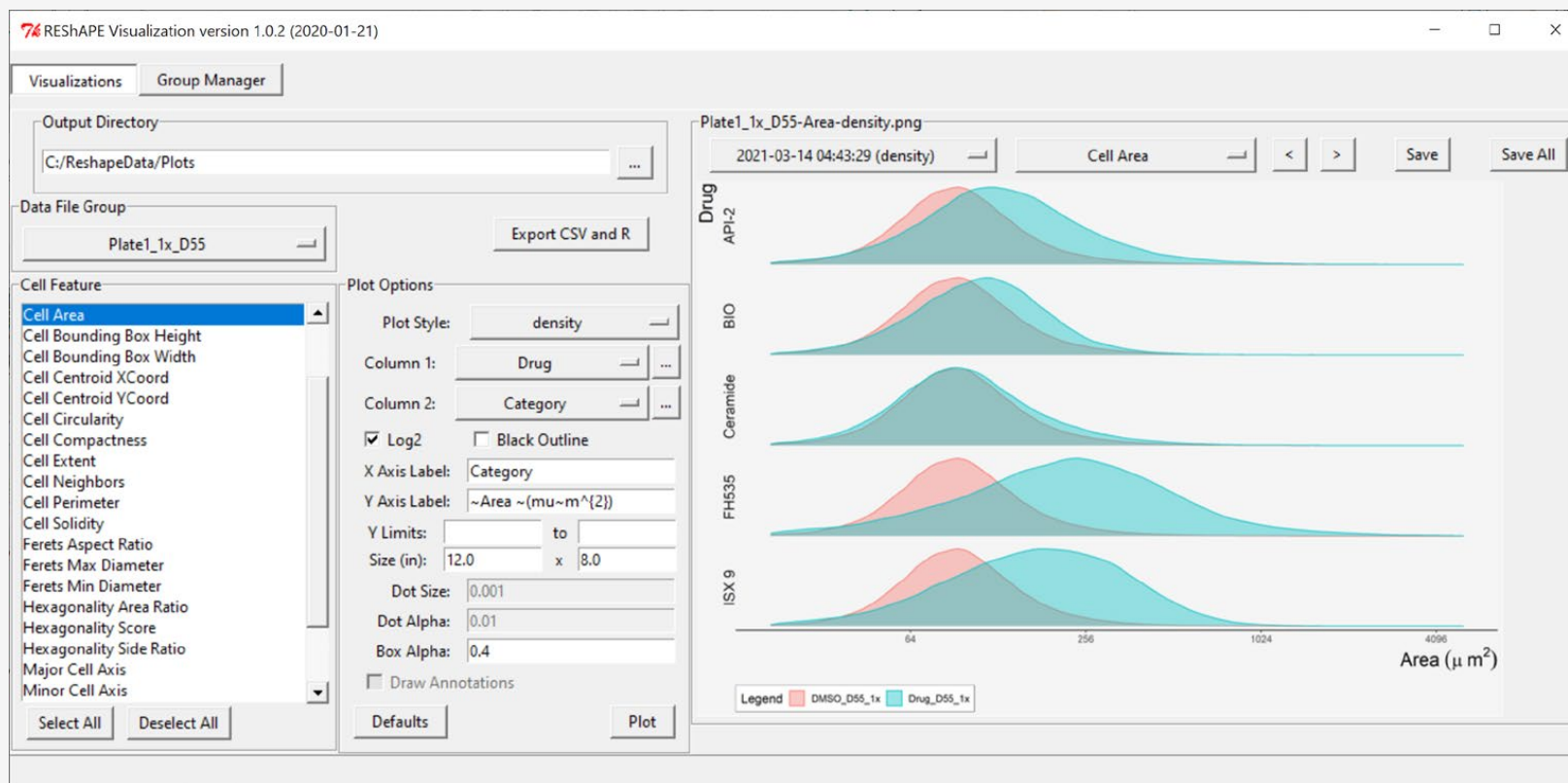
- Required switching between different external applications
- Some parts were painfully slow
- Limited image size (~30,000 x 30,000 pixels max)
- Did not support Carl Zeiss microscope images (CZI) directly

Updated process:

- Has a **unified UI** (pictured), no need for switching between external applications along the way
- **Slow parts were optimized**, now it takes minutes/hours instead of days/weeks
- **Supports extra large images**, the size is only limited by the amount of available RAM
- **Supports CZI**
- **Can be deployed to other systems, including Cloud VMs**



RESHAPE Visualizations



Automatically generates most common types of charts to visualize statistical distributions of cells by different geometrical parameters computed by RESHAPE.

Relevance to NEI (and outside)

RESHAPE is ready to be used by any lab which works on epithelia or cells with similar shape. Implementation on cloud will be very useful for making the software available.

RESHAPE can be extended/adapted for use on any other cell type

What's left to do?

RESHAPE is still dependent on MATLAB (and MATLAB licenses).

We are currently converting all RESHAPE code to Python to match the need of efficient cloud use and to optimize it for native cloud infrastructure.