

## Breakout Session 4: Track A

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

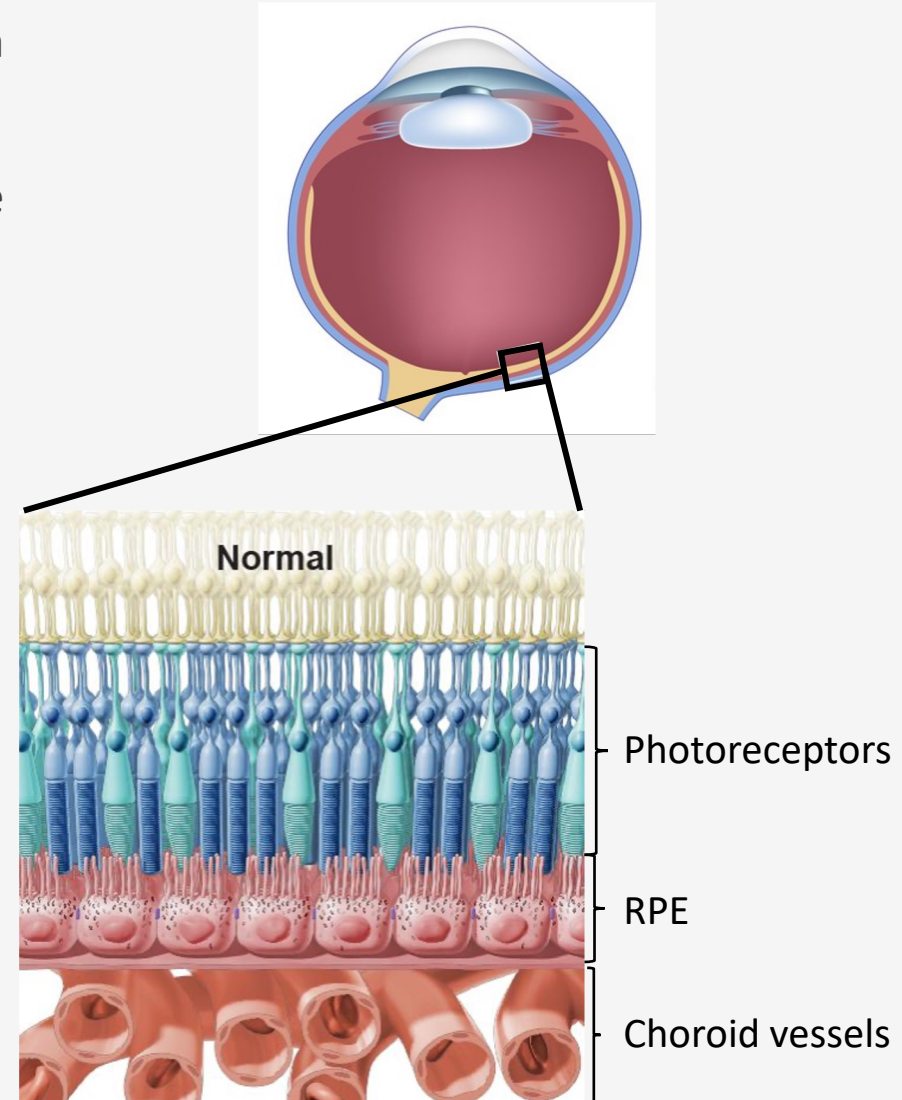
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*Postdoc, NEI/NIH*

# **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

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Normal Vision



AMD Vision



RP Vision

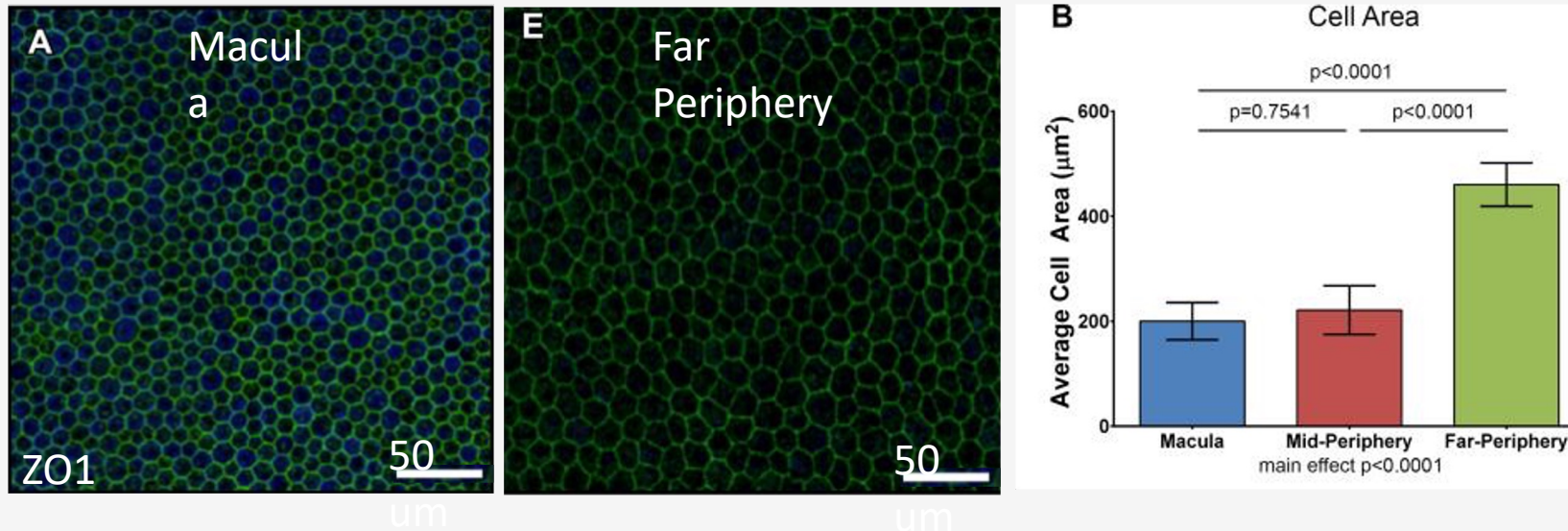


- Macular RPE degeneration leads to Age-related Macular Degeneration (AMD)
- Peripheral RPE defects leads to Retinitis Pigmentosa (RP) (RPE65 mutations)

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

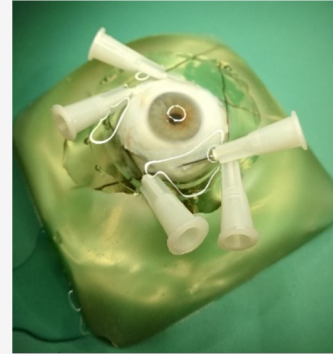
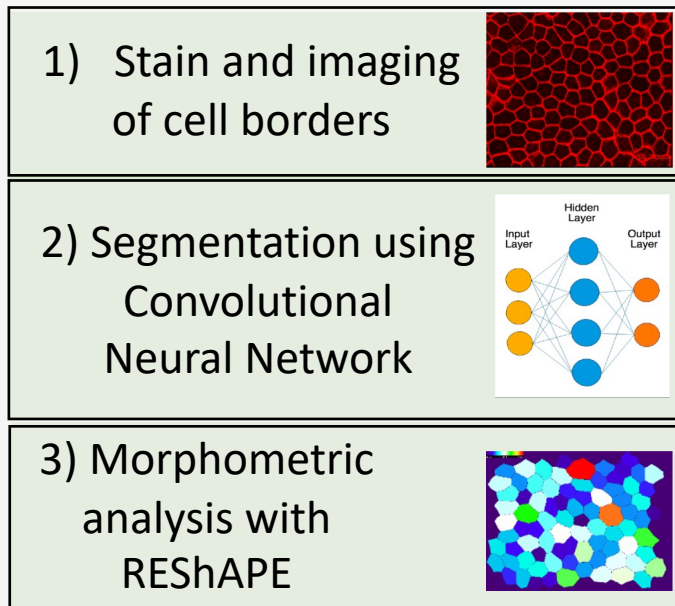
# Regional Differences in Retinal Pigment Epithelium (RPE)

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

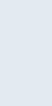


Compare human RPE morphometry

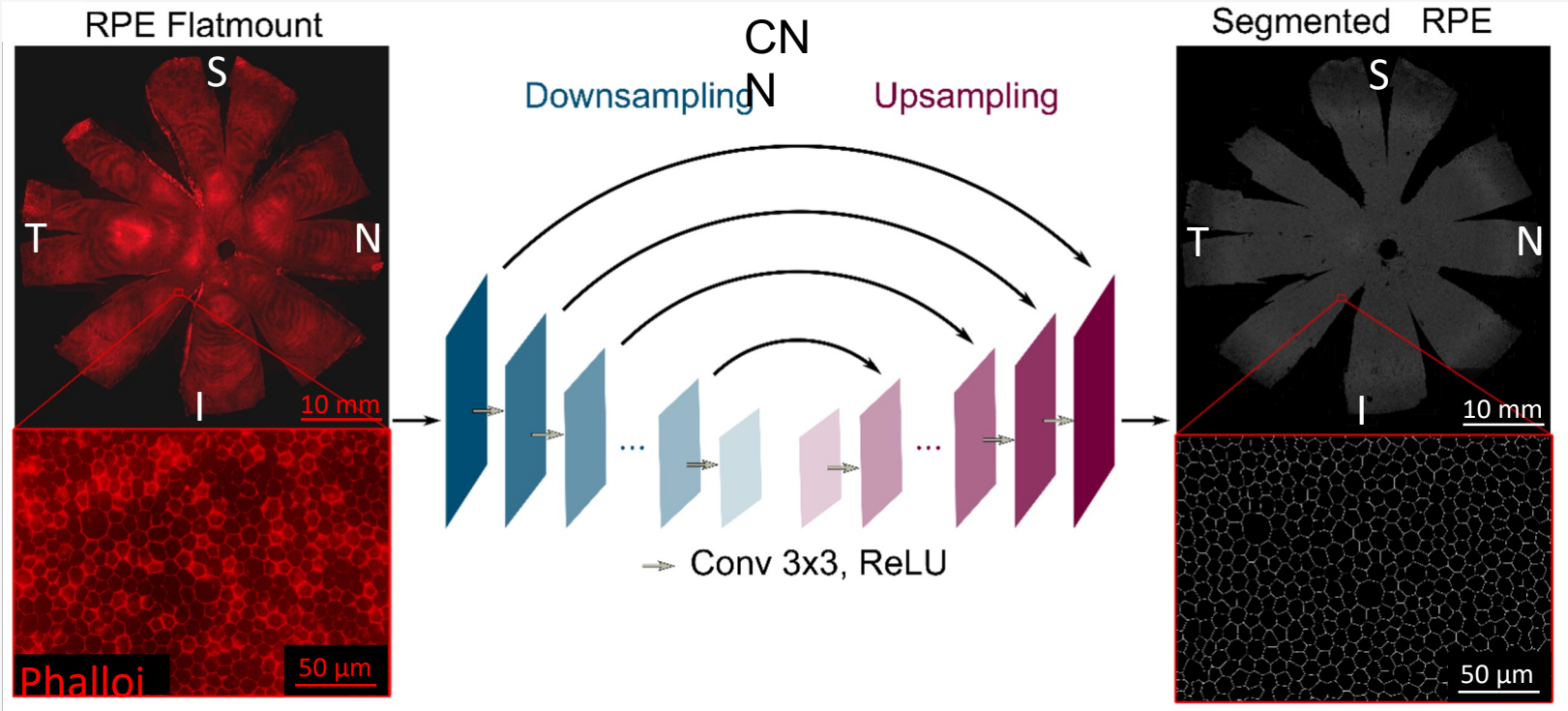
Peripheral RPE



Macular RPE



# Segmentation Using Convolutional Neural Network (CNN)



Phalloidin

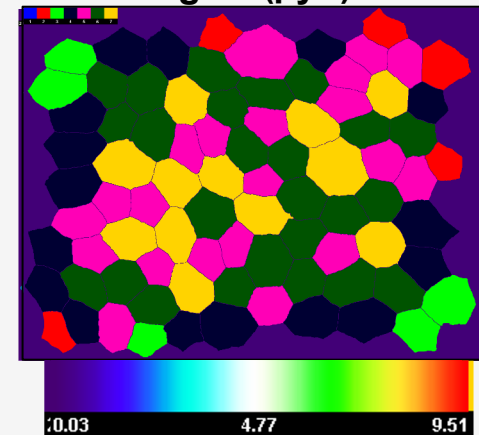
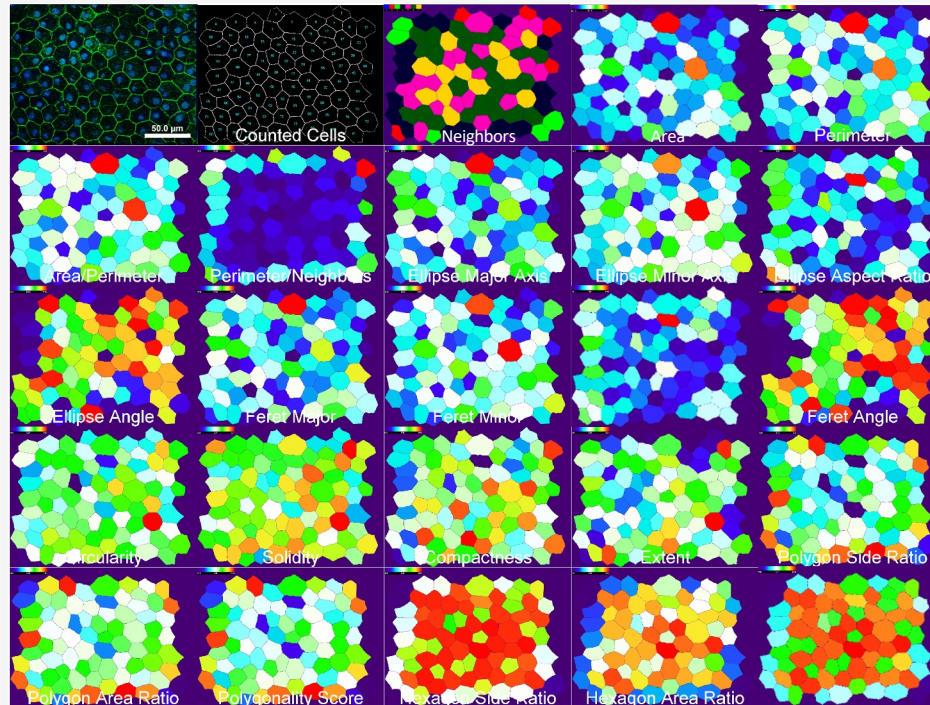
S = Superior  
N = Nasal  
I = Inferior

Segmentation accuracy 95-98%

# Morphometric Analysis with REShAPE

- Retinal Epithelium Shape And Pigment Evaluator

- 30 distinct shape metrics
- Creates a graphical heatmap of cell metrics

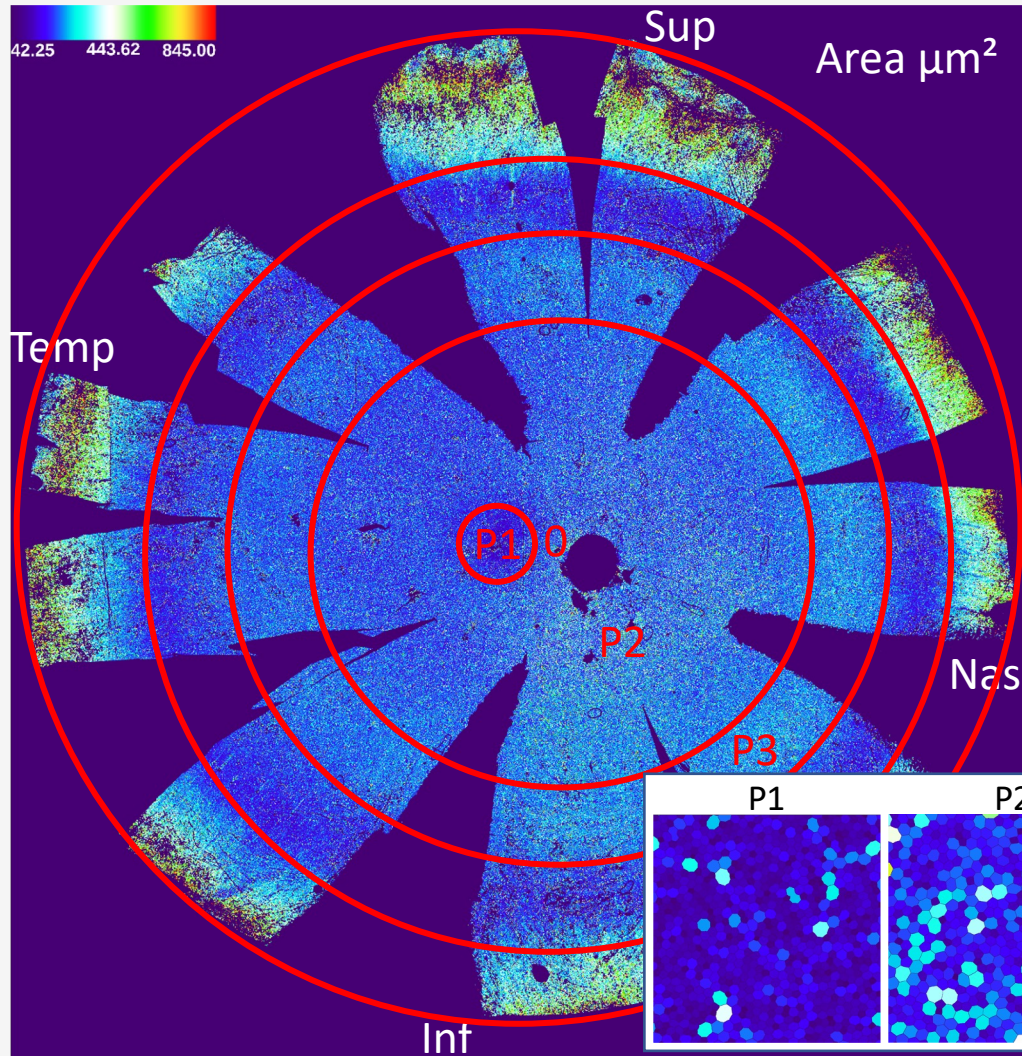


Worksheet  
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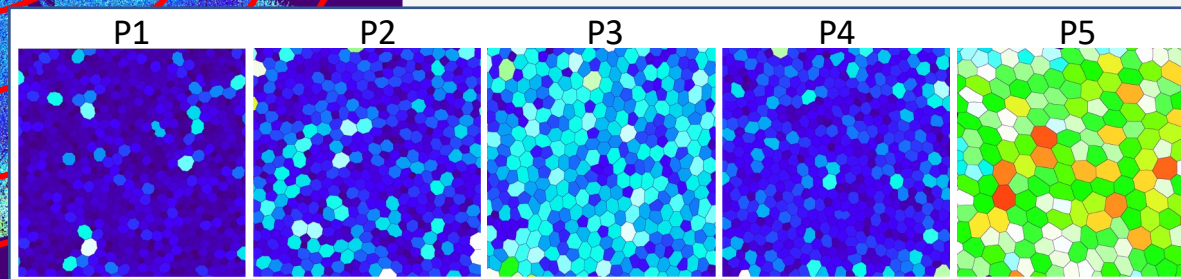
- Schaub and Hotaling et al, *Deep learning predicts function of live retinal pigment epithelium from quantitative microscopy*, Journal of Clinical Investigation, 2020
- Ortolan, D. et al. *Single-cell-resolution map of human retinal pigment epithelium helps discover subpopulations with differential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



# Morphometric Analysis 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



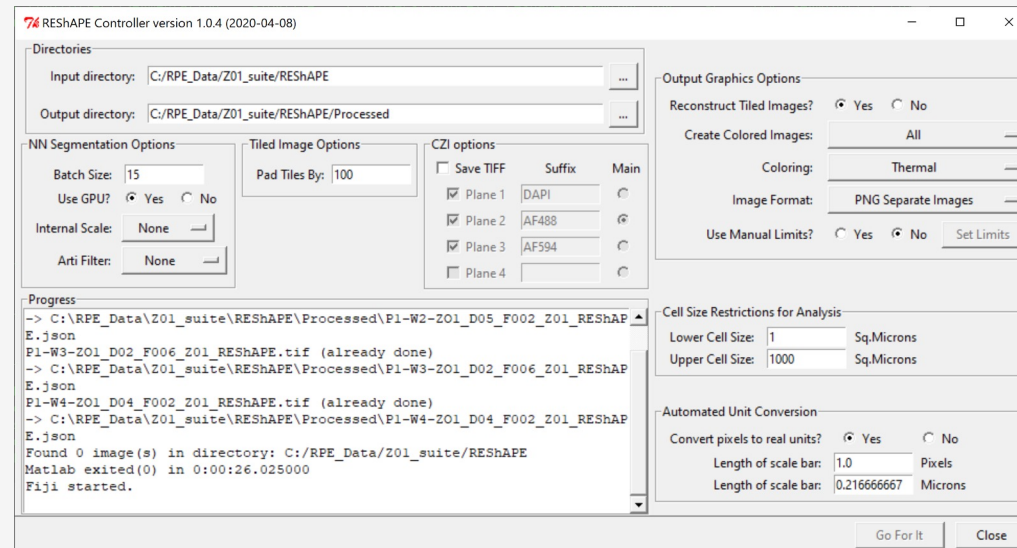
# Enhancements and Improvements to REShAPE processing from Strides Initiative

## Previous process:

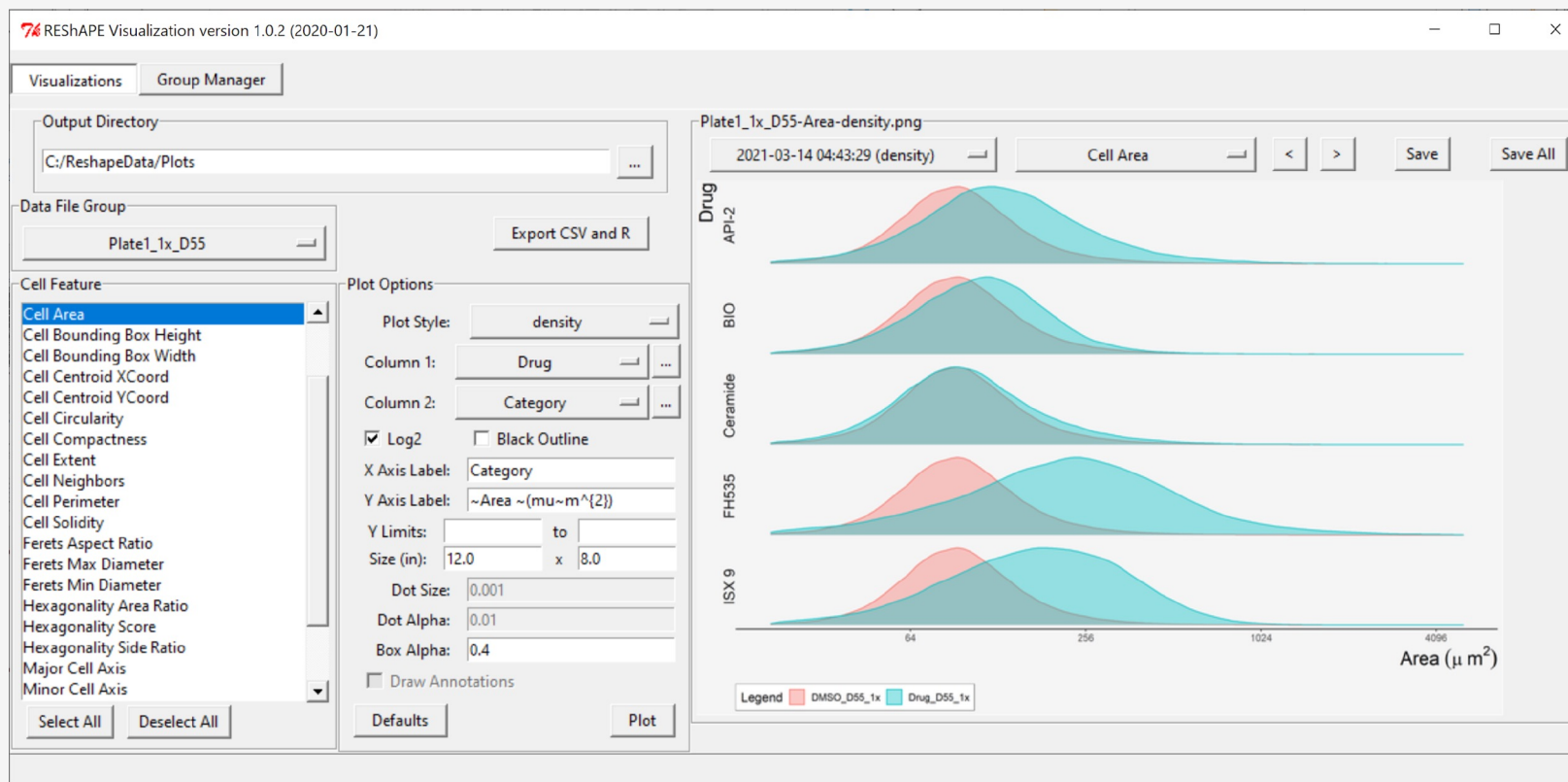
- Required switching between different external applications
- Some parts were painfully slow
- Limited image size (~30,000 x 30,000 pixels max)
- Did not support Carl Zeiss microscope images (CZI) directly

## 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)

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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.