Unraveling Optic Nerve Shapes: A Topological Dive into IIH through Fundus Photo Analysis

Josue Antonio
Consultant: Brad Turow

December 9, 2023

Motivation: Unraveling Optic Nerve Shapes in IIH

Idiopathic Intracranial Hypertension:
Rare condition impacting optic nerve, causing severe vision impairment.

Motivation: Unraveling Optic Nerve Shapes in IIH

Idiopathic Intracranial Hypertension:
Rare condition impacting optic nerve, causing severe vision impairment.
Incidence and Symptoms:
IIH incidence (about 1 in 100,000 people), symptoms include blurred vision, double vision, and vision loss.

Motivation: Unraveling Optic Nerve Shapes in IIH

Idiopathic Intracranial Hypertension:
Rare condition impacting optic nerve, causing severe vision impairment.
Incidence and Symptoms:
IIH incidence (about 1 in 100,000 people), symptoms include blurred vision, double vision, and vision loss.
Current Diagnostic Challenges:
Manual analysis limitations - laborious, time-consuming, subjective, and prone to errors.

Motivation: Unraveling Optic Nerve Shapes in IIH

Idiopathic Intracranial Hypertension:
Rare condition impacting optic nerve, causing severe vision impairment.

Incidence and Symptoms:
IIH incidence (about 1 in 100,000 people), symptoms include blurred vision, double vision, and vision loss.

Current Diagnostic Challenges:
Manual analysis limitations - laborious, time-consuming, subjective, and prone to errors.

Incidence Comparison:
IIH research gap compared to more prevalent diseases like glaucoma.

Motivation: Unraveling Optic Nerve Shapes in IIH

Idiopathic Intracranial Hypertension:
Rare condition impacting optic nerve, causing severe vision impairment.

Incidence and Symptoms:
IIH incidence (about 1 in 100,000 people), symptoms include blurred vision, double vision, and vision loss.

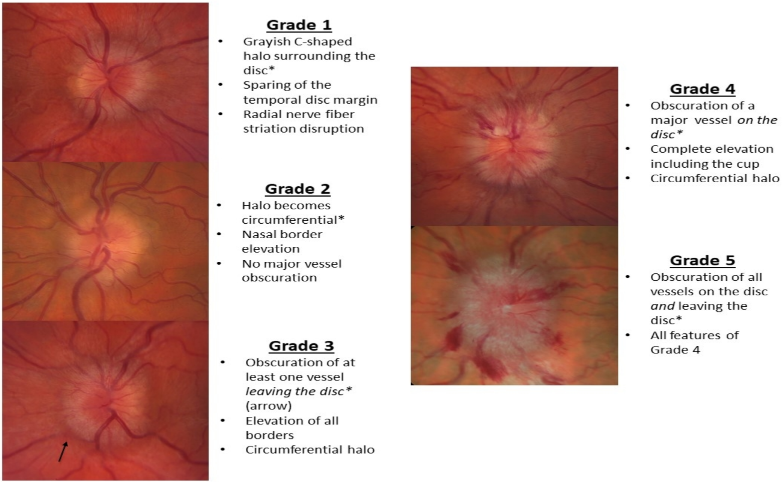
Current Diagnostic Challenges:
Manual analysis limitations - laborious, time-consuming, subjective, and prone to errors.

Incidence Comparison:
IIH research gap compared to more prevalent diseases like glaucoma.

Significance of Automated Diagnostics:
Urgency for automated methods due to drawbacks of manual analysis.

Background: IIH Diagnosis and Fundus Photography

Diagnostic Methods: Fundus photography; Frisen grade system (1 to 5) for severity assessment.



Data Source

- Dataset from Mount Sinai Hospital originated from the IIH Treatment Trial, the largest cohort of untreated IIH patients.
- 165 IIH patients from several sites in the US and Canada over 3 years.
- Fundus photography used in trial, capturing 6,566 images labeled with Frisen grades (0-5); Grade 0: Control group from healthy eyes.

Data Source cont'd

- Dataset exhibits significant class imbalance: Grade 5 accounts for less than two percent of the data, while grade 2 accounts for a third of the data.
- Preprocessing: Resized each fundus photo to 224x224 pixels and converted them to gray scale.

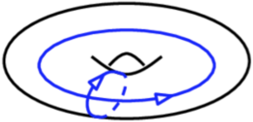
Topological Data Analysis (TDA)

- TDA employs algebraic topology to analyze high-dimensional, incomplete, and noisy datasets.
- Provides methods to study data structure using low-dimensional topological invariants such as homology.

Homology

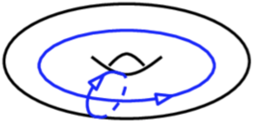
- **Homology:** Measures the presence of n-dimensional holes in a topological space.
- Connectedness (0-dimensional holes): Captured by H_0.
- Loops (1-dimensional holes): Captured by H_1.
- Voids (2-dimensional holes): Captured by H_2.
- For computational efficiency, our Python program will compute homology vector spaces using coefficients in $\mathbb{Z}_2$.

Persistent Homology and Homology



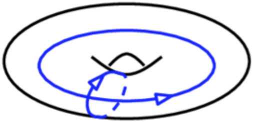
$$\begin{cases} \mathbf{H}_0(\mathbb{Z}_2) \cong \mathbb{Z}_2 \\ \mathbf{H}_1(\mathbb{Z}_2) \cong \mathbb{Z}_2 \oplus \mathbb{Z}_2 \\ \mathbf{H}_2(\mathbb{Z}_2) \cong \mathbb{Z}_2 \end{cases}$$

Persistent Homology and Homology



$$\begin{cases} \mathbf{H}_0(\mathbb{Z}_2) \cong \mathbb{Z}_2 \\ \mathbf{H}_1(\mathbb{Z}_2) \cong \mathbb{Z}_2 \oplus \mathbb{Z}_2 \\ \mathbf{H}_2(\mathbb{Z}_2) \cong \mathbb{Z}_2 \end{cases}$$

Question: How can we transform our data into a topological space?



$$\begin{cases} \mathbf{H}_0(\mathbb{Z}_2) \cong \mathbb{Z}_2 \\ \mathbf{H}_1(\mathbb{Z}_2) \cong \mathbb{Z}_2 \oplus \mathbb{Z}_2 \\ \mathbf{H}_2(\mathbb{Z}_2) \cong \mathbb{Z}_2 \end{cases}$$

Question: How can we transform our data into a topological space?
Answer: Simplicial Complexes!

Simplicial Complexes in TDA

1. n-simplices are the generalization of triangles to arbitrary dimensions (vertices, edges, triangles, tetrahedra, etc).

Definition (Simplicial Complex)

A simplicial complex K is a set of n-simplices such that:

1. Every face (sub-simplices) of a simplex in K is also in K.
2. The non-empty intersection of any two simplices $\sigma_1, \sigma_2 \in K$ is a face of both σ_1 and σ_2.

- For n-dimensional data, simplices can have dimensions up to n, with a focus on capturing $(n-1)$-dimensional and lower features.
- In our analysis of two-dimensional fundus photos, we focus on 0- and 1-dimensional features: (connected) components and loops.

Persistent Homology and Filtrations

- Each simplicial complex will correspond to a particular scale.
- The scale parameter of each complex depends on the data you're working with. For point cloud data (e.g., torus), this could be a distance threshold ϵ, and for $2D$ images this could be pixel intensity values as we will see shortly.

Persistent Homology and Filtrations

- Each simplicial complex will correspond to a particular scale.
- The scale parameter of each complex depends on the data you're working with. For point cloud data (e.g., torus), this could be a distance threshold ϵ, and for $2D$ images this could be pixel intensity values as we will see shortly.
- **Filtrations:** Collection of subcomplexes K_i of some complex K such that if $i \leq j$, then $K_i \subseteq K_j$. Here i and j represent different scales.

Persistent Homology and Filtrations

- Each simplicial complex will correspond to a particular scale.
- The scale parameter of each complex depends on the data you're working with. For point cloud data (e.g., torus), this could be a distance threshold ϵ, and for $2D$ images this could be pixel intensity values as we will see shortly.
- **Filtrations:** Collection of subcomplexes K_i of some complex K such that if $i \leq j$, then $K_i \subseteq K_j$. Here i and j represent different scales.
- **Persistent Homology:** Captures how topological features persist across different scales, i.e., how homology vector spaces change from one complex to another.

Topologizing Fundus Photos

Definition (Sublevel Set)

Let $c \in \mathbb{R}$ and $f : \mathbb{R}^n \to \mathbb{R}$, then

$$L_c(f) = \{(x_1, \cdots, x_n) : f(x_1, \cdots, x_n) \leq c\}$$

is the sublevel set of f.

One way of topologizing our data is by constructing simplicial complexes according to the sublevel sets of the following function

$$f : V \to [0, 255]$$

where V is the set of vertices/pixels of a given photo, and the codomain represents the range of possible pixel intensity values (gray scale).

Topologizing Fundus Photos cont'd

- Start with an image I and an empty complex K.

Topologizing Fundus Photos cont'd

- Start with an image I and an empty complex K.
- Assign pixels to vertices (0-simplices) in I and add them to K.

Topologizing Fundus Photos cont'd

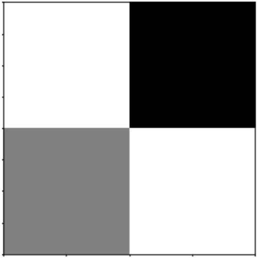
- Start with an image I and an empty complex K.
- Assign pixels to vertices (0-simplices) in I and add them to K.
- Add line segments (1-simplices) between adjacent vertices (include diagonally adjacent).

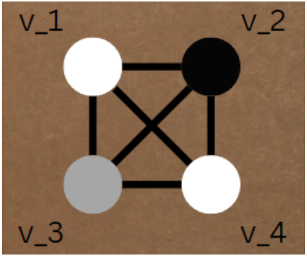
Topologizing Fundus Photos cont'd

- Start with an image I and an empty complex K.
- Assign pixels to vertices (0-simplices) in I and add them to K.
- Add line segments (1-simplices) between adjacent vertices (include diagonally adjacent).
- Result: K, a fully-connected simplicial complex of I.

Topologizing Fundus Photos cont'd

- Start with an image I and an empty complex K.
- Assign pixels to vertices (0-simplices) in I and add them to K.
- Add line segments (1-simplices) between adjacent vertices (include diagonally adjacent).
- Result: K, a fully-connected simplicial complex of I.





Sublevel Set Filtration

Now we define subcomplexes and construct the sublevel set filtration on the pixel intensity function f. Let K be the fully-connected complex containing all vertices in I. Then:

$$K_i = \{\sigma \in K : \forall v \in \sigma, f(v) \leq i\}.$$

Definition (Sublevel Set Filtration)

Let $a_0 = f_{min} < a_1 < a_2 \cdots < a_n = f_{max}$ be an increasing sequence of positive real numbers, then the sequence of subcomplexes: $K_{f_{min}=0} \subseteq K_{0+a_1} \subseteq K_{0+a_2} \subseteq \cdots \subseteq K_{f_{max}=255} = K$ is a *filtration* of K called the sublevel set filtration.

Sublevel Set Filtration cont'd

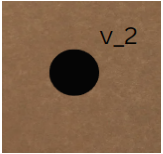


Figure: $K_0 = \{v_2\}$

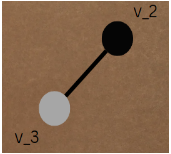


Figure: $K_{127.5} = \{v_2, v_3\}$

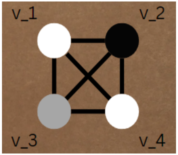


Figure: $K_{255} = K$

Let $0 < 127.5 < 255$ be the increasing sequence , then:
$K_0 = \{\sigma \in K : \forall v \in \sigma, f(v) \leq 0\} = \{v_2\}$ only v_2 is dim enough.
$K_{127.5} = \{\sigma \in K : f(v) \leq 127.5\} = \{v_2, v_3\}$ v_2 and v_3 are dim enough.
$K_{255} = \{\sigma \in K : f(v) \leq 255\} = \{v_1, v_2, v_3, v_4\}$ all pixels are dim enough and we get the fully-connected simplex K.

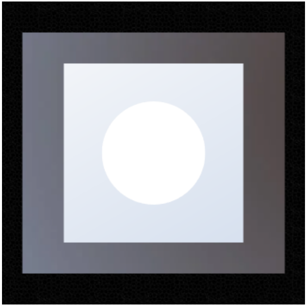
Birth and Death in Topological Features

- After constructing each complex for an intensity scale, homology vector spaces are computed.

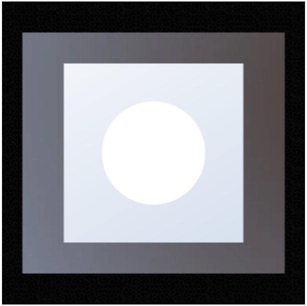
Birth and Death in Topological Features

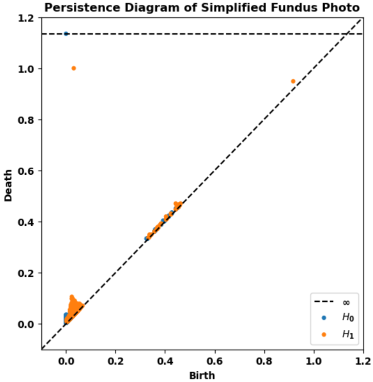
- After constructing each complex for an intensity scale, homology vector spaces are computed.
- Changes in homology across all complexes are visually represented by Persistence Diagrams.

Simplified Fundus Photo and Persistence Diagram

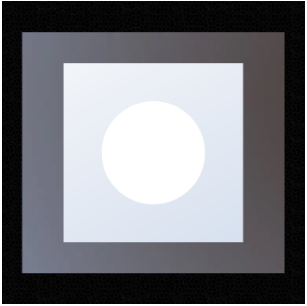


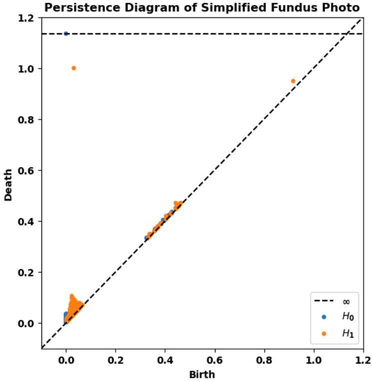
Simplified Fundus Photo and Persistence Diagram





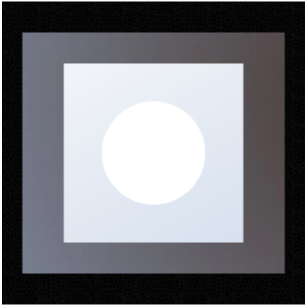
Simplified Fundus Photo and Persistence Diagram

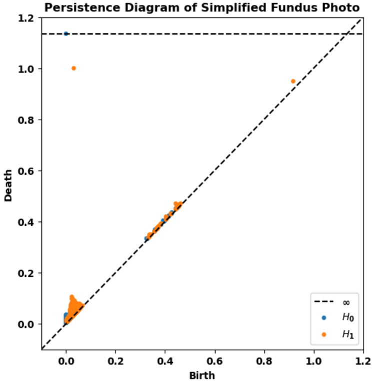




- **Dimension 0:** One persistent point at infinity, representing a connected component (e.g., black square) that persists throughout.

Simplified Fundus Photo and Persistence Diagram





- **Dimension 0:** One persistent point at infinity, representing a connected component (e.g., black square) that persists throughout.
- **Dimension 1:** One persistent point with high *death* value, indicating the presence of a loop (e.g., boundary of the white circle) persisting across intensity levels.

Understanding Persistence Diagrams

- A persistence diagram is a 2D representation of feature's lifetimes.
- Each point is a (born, death) pair, with x as the birth scale and y as the death scale.
- Features (components or loops) are *born* when first captured at some scale and *die* when no longer present, i.e., scale when they disappear.
- Points with high y-values, well above the diagonal, signify persistent features associated with significant topological structures.
- Points near the diagonal represent features with short lifespans, indicating rapid changes or less influential variations.

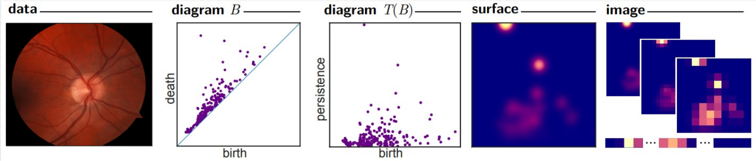
Featurization with Persistence Images

- **Objective:**
  - Extract machine learning-friendly features from persistence diagrams.

Featurization with Persistence Images

- **Objective:**
  - Extract machine learning-friendly features from persistence diagrams.
- **Limitations of Raw Persistence Diagrams:**
  - Not directly suitable for machine learning methods.
  - Reason: Lack of inherent Euclidean structure, i.e., inner products.
  - Need for a transformation process.

Persistence Image: A Brief Overview



- **Featurization Steps:**
  - Birth-death coordinates to birth-persistence coordinates.
  - Definition of a differentiable probability distribution.
  - Introduction of a nonnegative weighting function.
  - Derivation of the persistence surface.
  - Definition of the persistence image.

Featurization Details

- **Featurization Steps:**
  - *Birth-death to Birth-persistence:*
    - Let $D = \{(a_i, b_i)\}_{i \in I}$ be a persistence diagram.
    - Define $T : \mathbb{R}^2 \to \mathbb{R}^2$ as $T(a, b) = (a, b - a)$.
    - $T(D)$ is the transformed multiset in birth-persistence coordinates.
  - *Probability Distribution:*
    - Let $\phi_u : \mathbb{R}^2 \to \mathbb{R}$ be a differentiable probability distribution with mean $u = (u_a, u_b) \in \mathbb{R}^2$.
    - Choose $\phi_u = g_u$ with $g_u(a, b) = \frac{1}{2\pi\sigma^2} e^{-\frac{(a-u_a)^2+(b-u_b)^2}{2\sigma^2}}$.

Transformation Details cont'd

- **Featurization Steps:**
  - *Weighting Function:*
    - Fix a nonnegative weighting function $f : \mathbb{R}^2 \to \mathbb{R}$ that's zero along the horizontal axis, continuous, and piecewise differentiable.
    - For example, $f_n(a, b) = b^n$ with $n \in \mathbb{Z}^+$ for assigning more weight to persistent features.
  - *Persistence Surface:*
    - Define the persistence surface $\rho_D : \mathbb{R}^2 \to \mathbb{R}$ as $\rho_D(z) = \sum_{u \in T(D)} f(u)\phi_u(z)$.

Definition

Let D be a persistence diagram, then its persistence image is defined as the collection of pixels $I(\rho_D)_p$ given by:

$$I(\rho_D)_p = \iint_p \rho_D \, db \, da.$$

Summary: Feature Extraction Pipeline

- **Feature Extraction Pipeline:**
  1. From each fundus photo, we construct a sublevel set filtration based on pixel intensity values.

Summary: Feature Extraction Pipeline

- **Feature Extraction Pipeline:**
  1. From each fundus photo, we construct a sublevel set filtration based on pixel intensity values.
  2. Compute the persistence diagram, capturing topological features.

Summary: Feature Extraction Pipeline

- **Feature Extraction Pipeline:**
  1. From each fundus photo, we construct a sublevel set filtration based on pixel intensity values.
  2. Compute the persistence diagram, capturing topological features.
  3. Transform the persistence diagram into a persistence image.

Summary: Feature Extraction Pipeline

- **Feature Extraction Pipeline:**
  1. From each fundus photo, we construct a sublevel set filtration based on pixel intensity values.
  2. Compute the persistence diagram, capturing topological features.
  3. Transform the persistence diagram into a persistence image.
  4. Flatten the persistence image to obtain a feature vector.

Summary: Feature Extraction Pipeline

- **Feature Extraction Pipeline:**
  1. From each fundus photo, we construct a sublevel set filtration based on pixel intensity values.
  2. Compute the persistence diagram, capturing topological features.
  3. Transform the persistence diagram into a persistence image.
  4. Flatten the persistence image to obtain a feature vector.
- **Machine Learning Objective:**
  - Build a classification model to predict disease severity grade, given an unlabeled fundus photo.

Random Forests: A Brief Overview

- **Random Forests:**
  - Ensemble learning method that builds multiple decision trees during training.
  - Each tree "votes" on the final classification, and the most popular choice is selected.
- **Key Features:**
  - Randomly selects a subset of features for each tree, promoting diversity.
  - Reduces overfitting and increases robustness by aggregating predictions.
- **Strengths:**
  - Suitable for complex datasets with high dimensionality.
  - Handles non-linear relationships and captures intricate patterns.
- **Application in Classification:**
  - Well-suited for image classification tasks, leveraging the power of multiple trees.

Results: Machine Learning with Random Forests

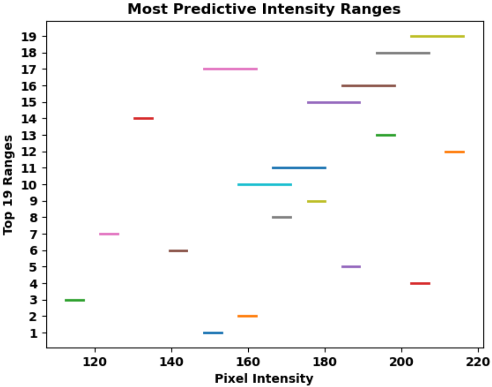
- **Data Preprocessing:**
  - Combined grade 4 and grade 5 images to address significant data imbalance.

Results: Machine Learning with Random Forests

- **Data Preprocessing:**
  - Combined grade 4 and grade 5 images to address significant data imbalance.
- **Current Best Classifier:**
  - Accuracy is a percentage representing correct predictions over the total number of samples.
  - Achieved a 62% accuracy in classifying Frisen grades.

rf4_hyperparams.png

- **Random Forests's Feature Importances Method:**
  - Identified most *predictive* components of persistence image vectors.
  - Importance was quantified as a fraction representing the contribution to the model's final prediction.
  - Each *predictive* feature corresponds to a specific range of pixel intensities in the original gray scale photos.



Most Important Features (Cont'd)

- **Top Most Predictive Pixel Intensity Ranges:**
  - Top 19 features (out of 841), collectively accounting for 20% of importance in prediction, were selected for further analysis.

- **Top Most Predictive Pixel Intensity Ranges:**
  - Top 19 features (out of 841), collectively accounting for 20% of importance in prediction, were selected for further analysis.

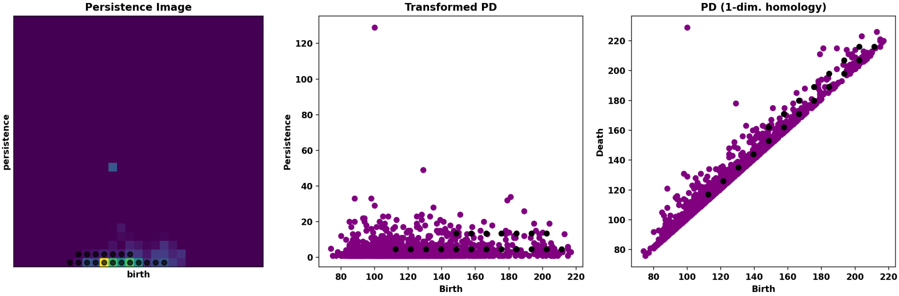


Figure: Selected Grade 4 Persistence Image with top 19 most predictive features overlaid.

Results (Cont'd): Visualizing Predictive Intensity Ranges

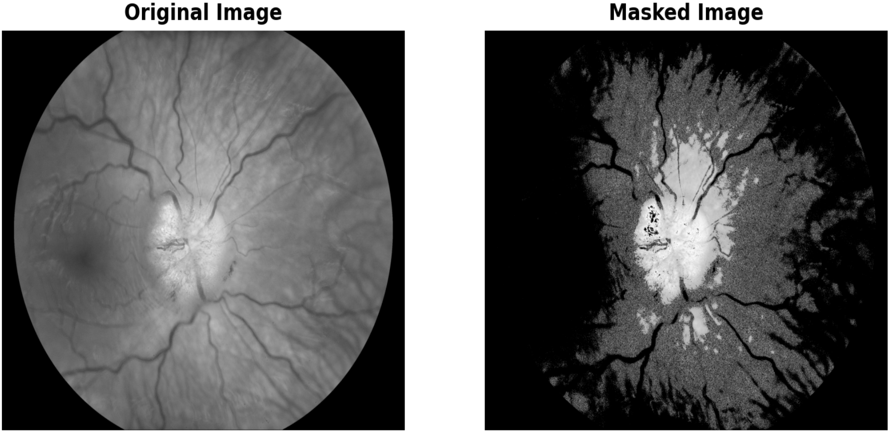
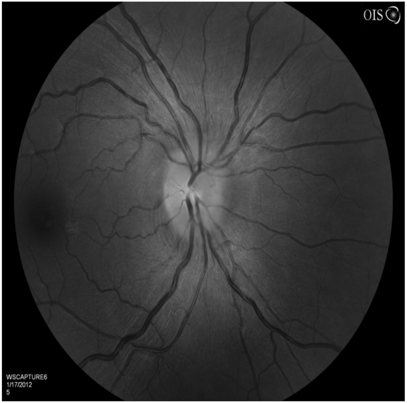


Figure: Pixels shown correspond to the top 19 intensity ranges in the previous persistence image.

Visualizing Predictive Intensity Ranges (Cont'd):

Original Image



Masked Image

Figure: Pixels shown correspond to the top 19 intensity ranges for selected grade 2 image.

Moving Forward

- Investigate methods for masking groups of photos instead of individual images.

Moving Forward

- Investigate methods for masking groups of photos instead of individual images.
- Work with colored images by splitting them into three channels. Apply the analysis procedure independently to each channel to leverage color information.

Moving Forward

- Investigate methods for masking groups of photos instead of individual images.
- Work with colored images by splitting them into three channels. Apply the analysis procedure independently to each channel to leverage color information.
- Consider different types of filtration.

Moving Forward

- Investigate methods for masking groups of photos instead of individual images.
- Work with colored images by splitting them into three channels. Apply the analysis procedure independently to each channel to leverage color information.
- Consider different types of filtration.
- Explore multi-parameter persistence for a comprehensive topological analysis. Consider combining pixel intensity with additional parameters for enhanced insights.

Thank you!!
Questions?