Multi-scale Looping and Branching Analysis of Brain Artery Trees

Alex Pieloch

Duke University (at time of research)

joint with

Paul Bendich, Ezra Miller (Duke), J.S. Marron & Sean Skwerer (Chapel Hill)

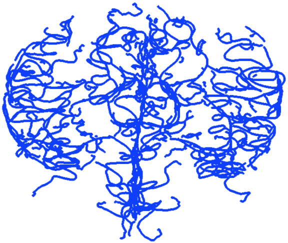
SHP - Fall 2019 - Topics in Topology
December 14, 2019

Acknowledgments

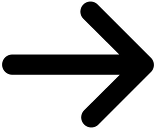
- Research was funded by NSF Research Training Grant "Structure in Complex Data".
- I thank the Information Initiative at Duke (now the Rhodes Information Initiative at Duke) for hosting me and providing a workspace.
- I thank Paul Bendich for his mentoring on this project.

Workflow

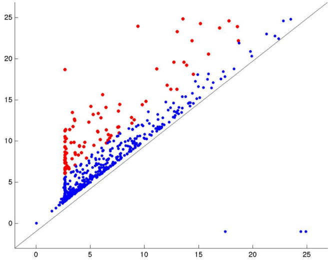
Brain Artery Trees



(Topological Data Analysis)



Persistence Diagrams



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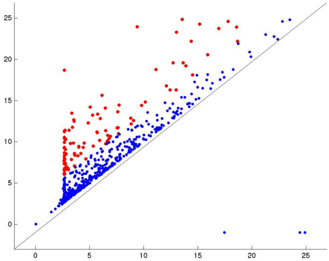
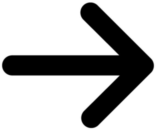
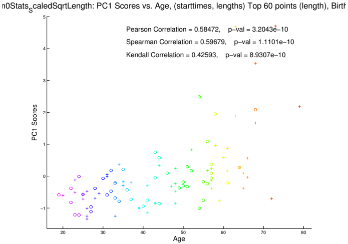


(Feature Extraction and Statistical Analysis)



Statistical Summaries



Goals

- Use Topological Data Analysis (TDA) to analyze the multi-scale geometry and topology of branching and looping structures in brain artery trees

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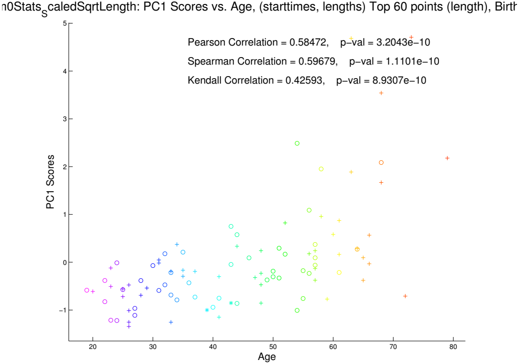
- Statistically analyze the 3D motifs that are identified by TDA in relation to covariates (age, sex, etc.)

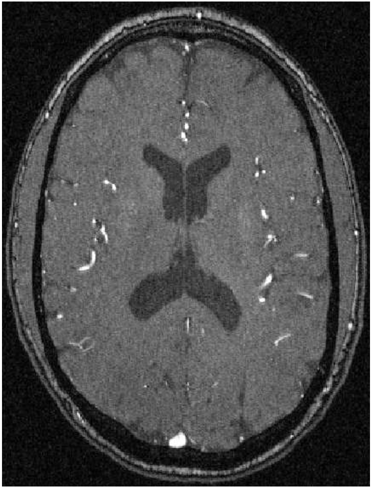
Results

Correlate quantified topological motifs with age. Pearson Correlation: **0.58**

p-value: $\mathbf{3.2043 \times 10^{-10}}$



Data Set



- Magnetic Resonance Angiography (MRA)

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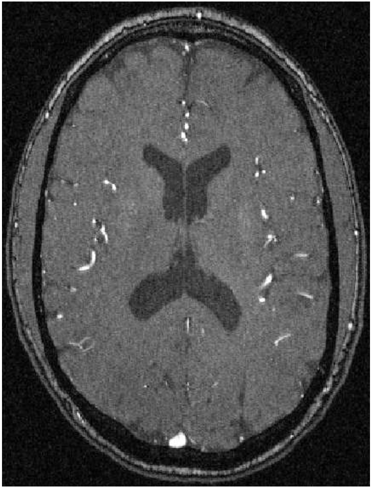

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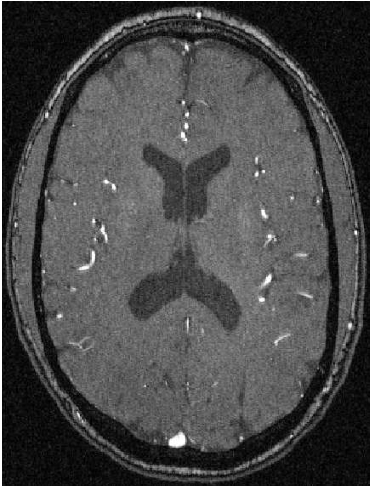
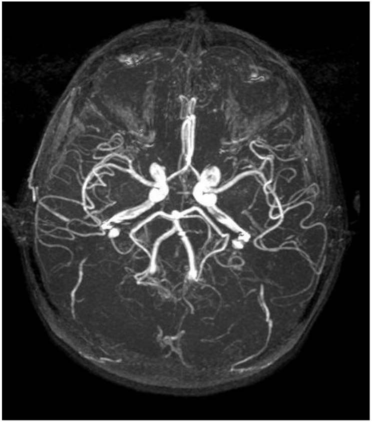


- Magnetic Resonance Angiography (MRA)
- Provided by Dr. Elizabeth Bullitt, Department of Neurosurgery at UNC- Chapel Hill
- Composed of 98 healthy subjects
- Roughly even mix of males and females
- Wide range of ages (18-77)

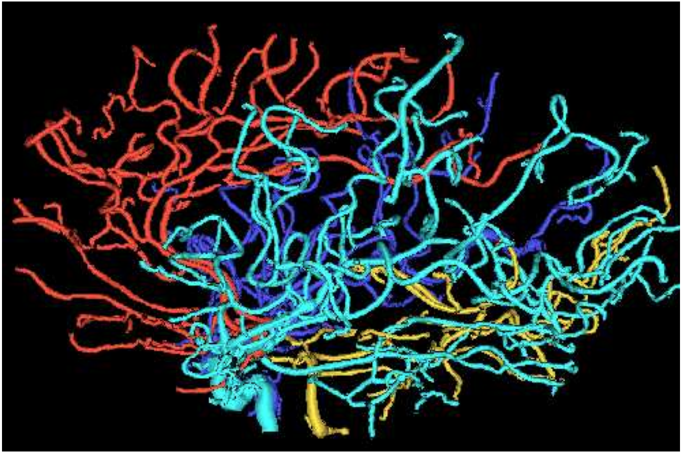
Magnetic Resonance Angiography

(Advanced Imaging of Port Charlotte)



(Imaging Group of Delaware)

Tube Tracking



(Bullitt-Aylward, 2002)

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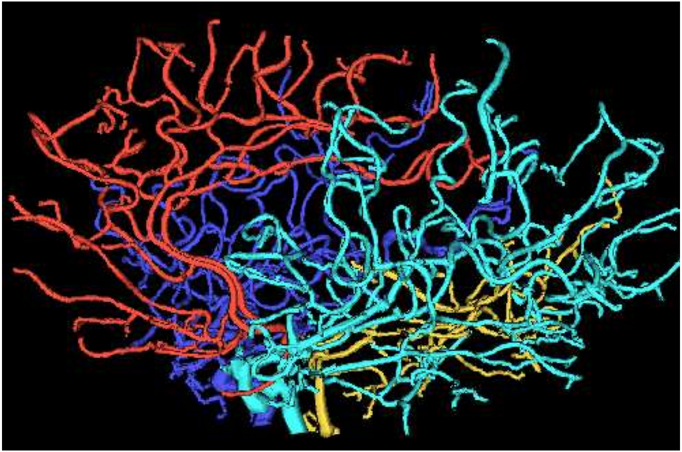

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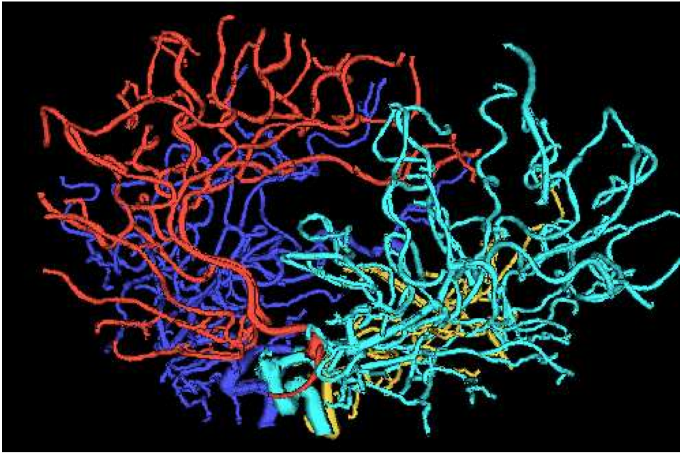

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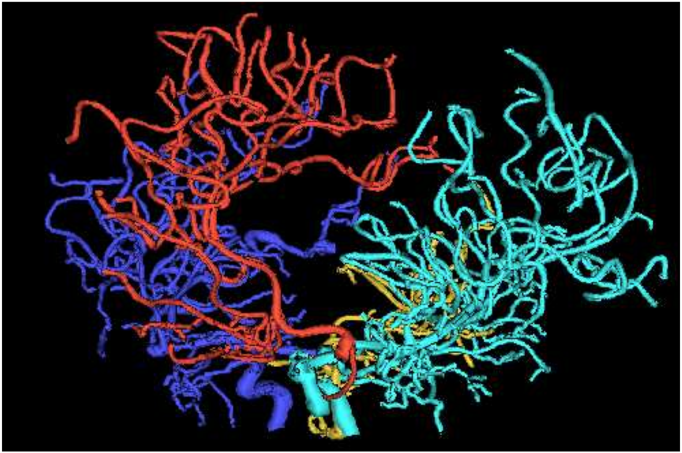

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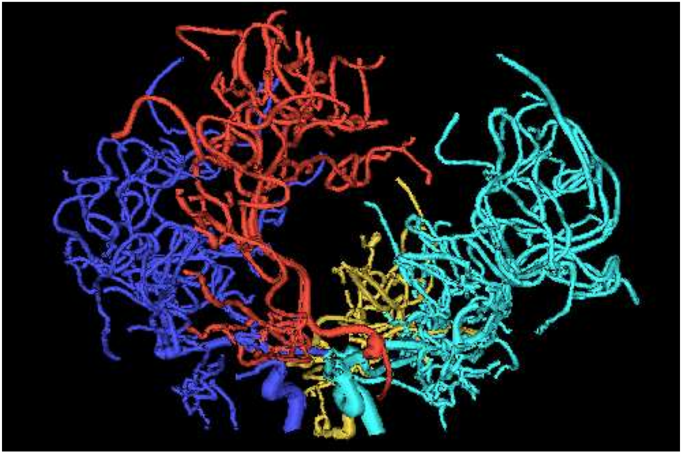

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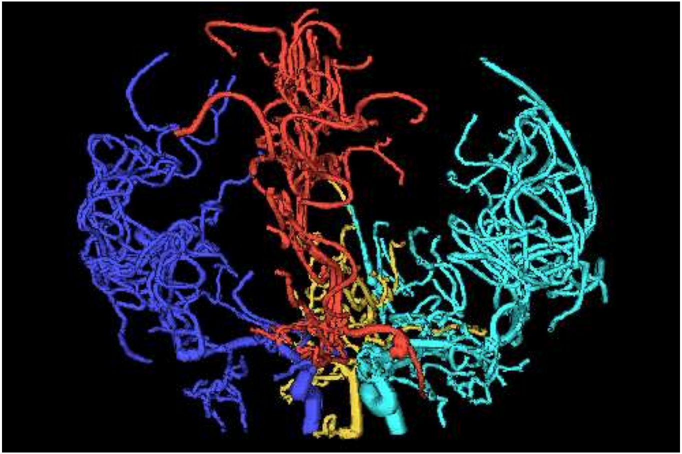

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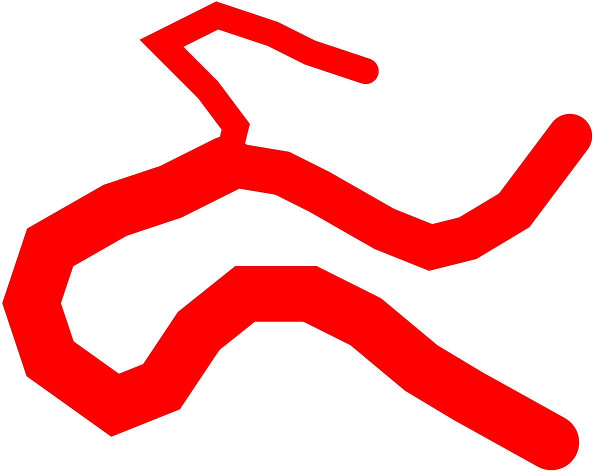

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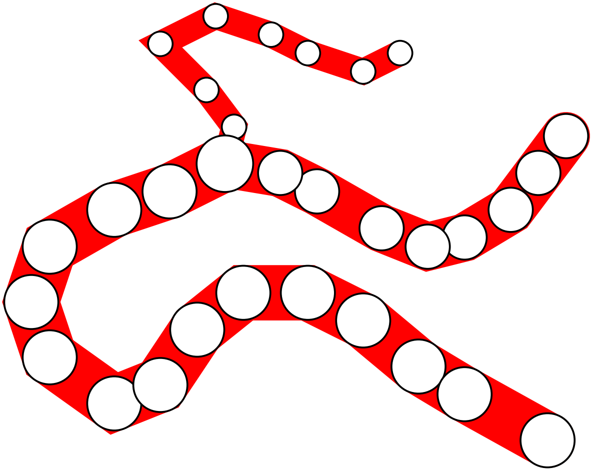

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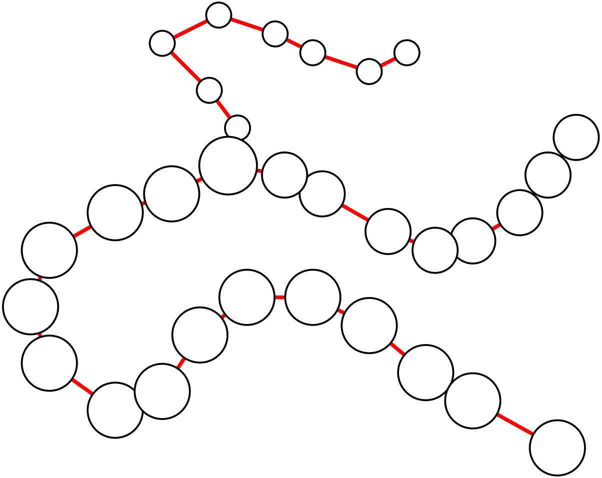

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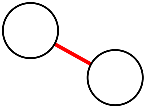

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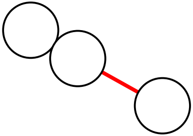

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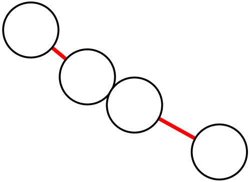

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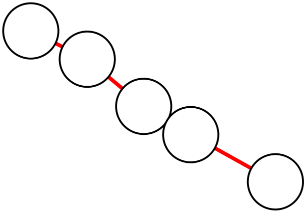

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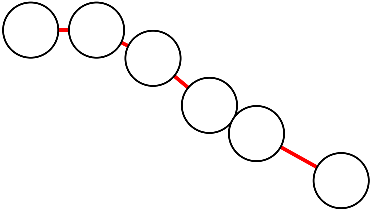

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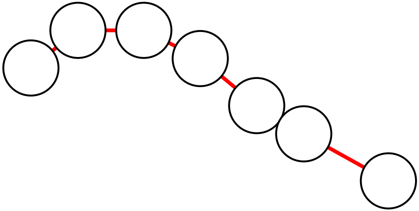

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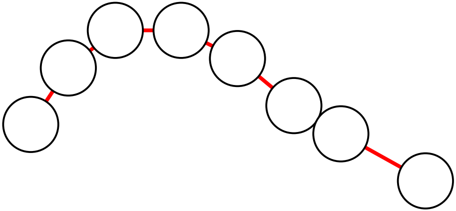

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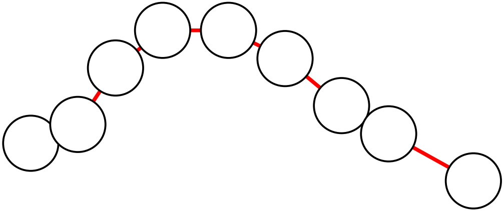

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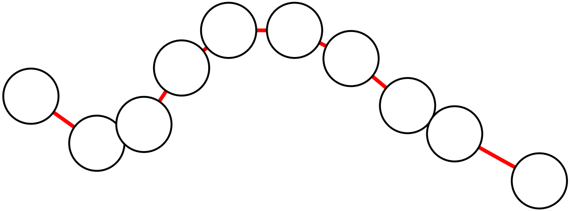

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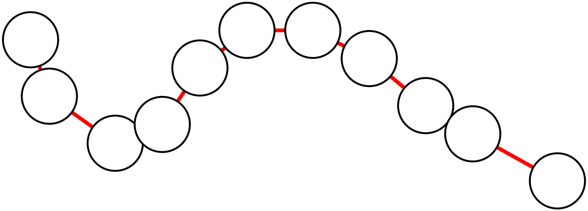

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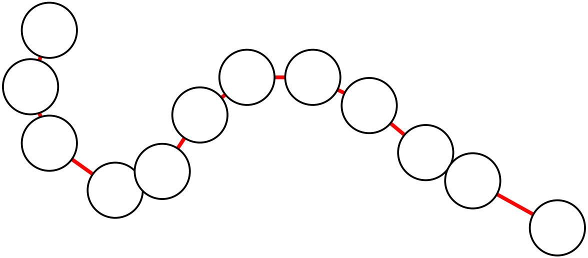

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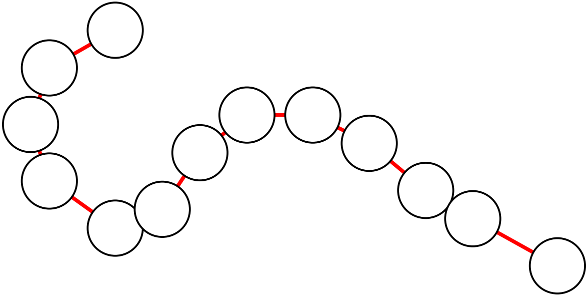

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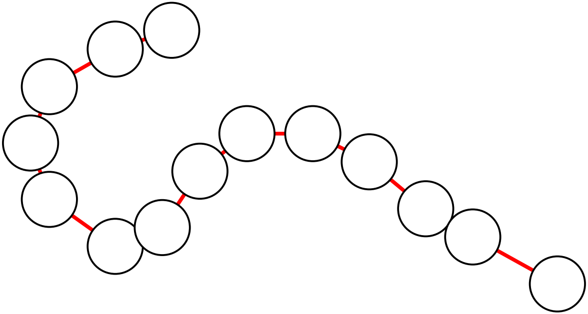

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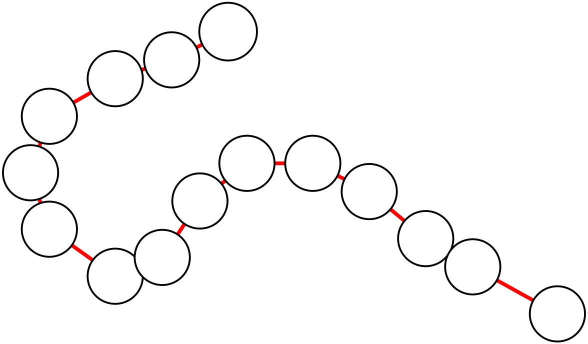

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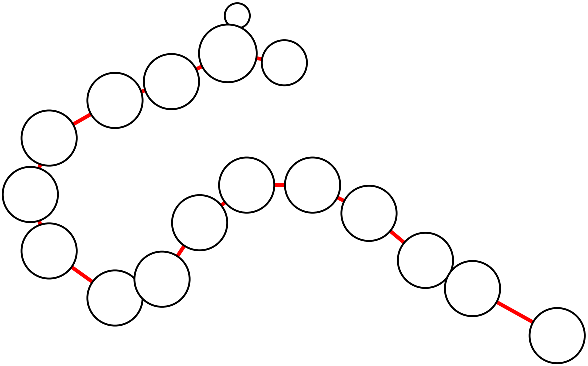

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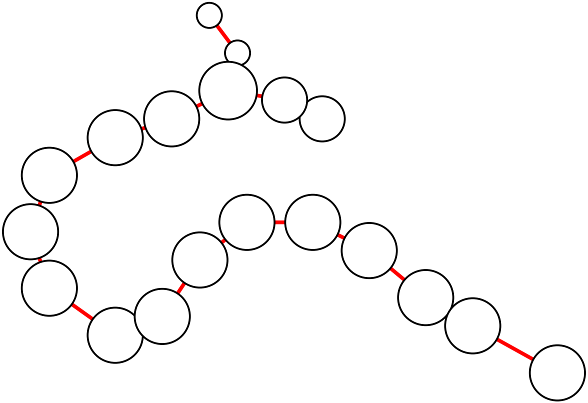

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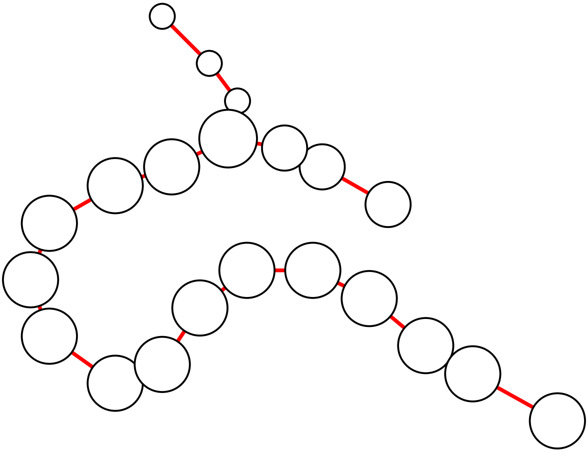

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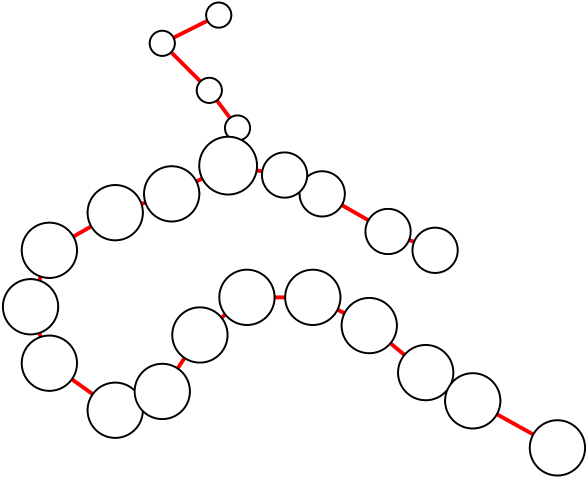

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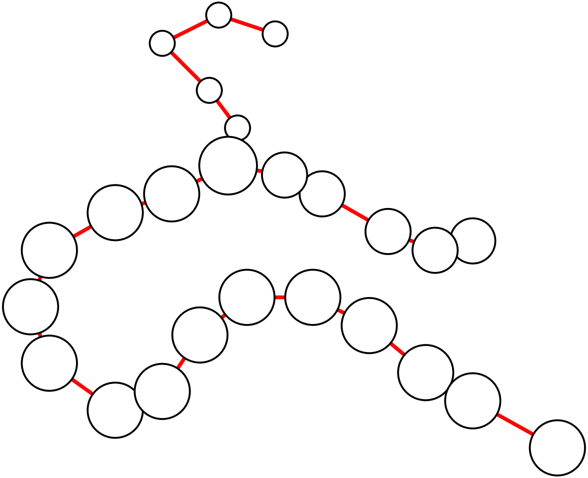

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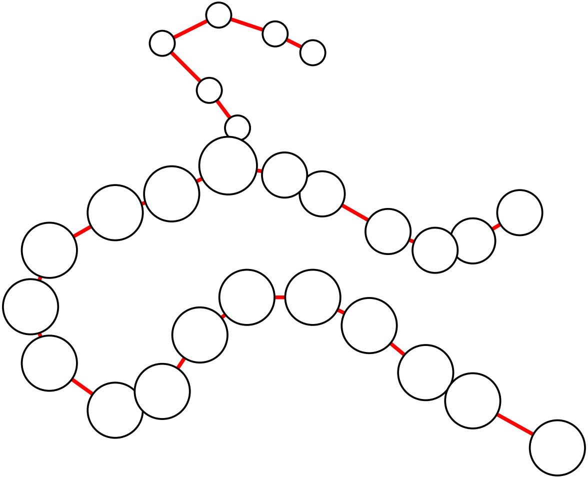

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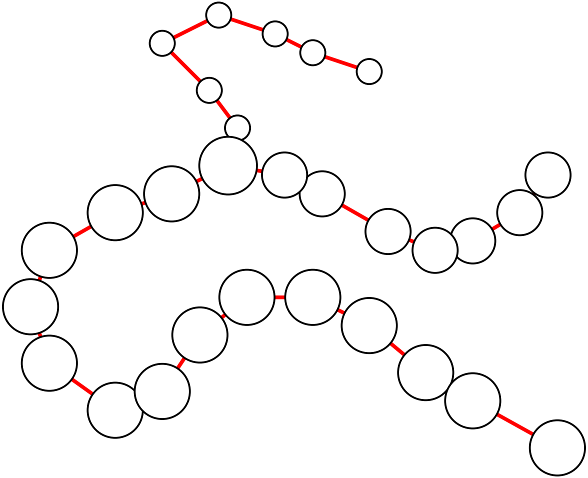

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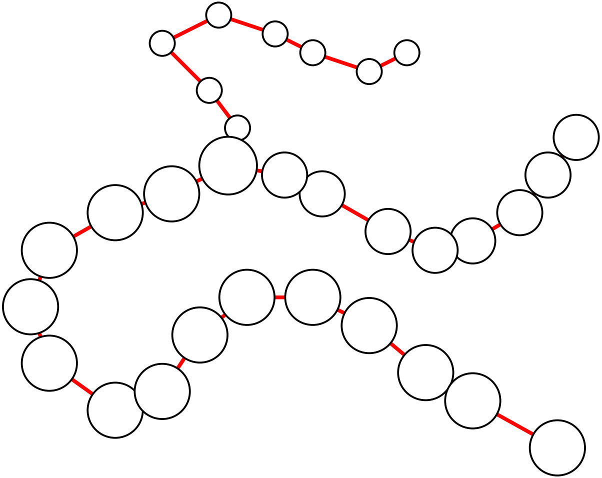

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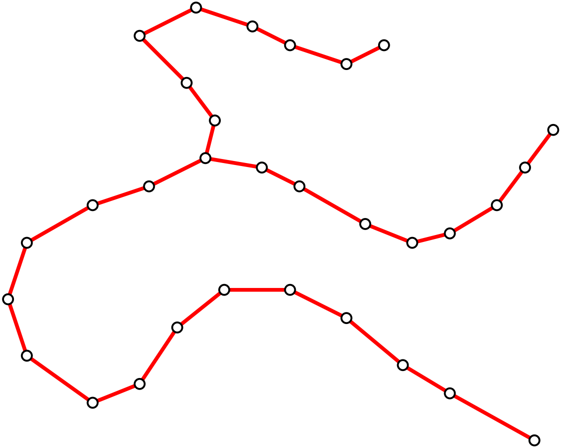

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- Apply averaging algorithm in tree space
- Found significant age and gender effects (some where stronger than previous analyses)

Moral of the story from previous analyses

- Combinatorics of branching patterns and branching length is not enough
- Need to analyze **geometry** of brain artery trees in 3D embedding

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- Combinatorics of branching patterns and branching length is not enough
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- Tortuosity!
  - How do the arteries wrap in on themselves?
  - Bending structure is important

Our Analysis

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- Use Topological Data Analysis (TDA) to quantify branching and looping structure of brain artery trees
- Big ideas:
  - "Filter" brain artery trees to find bends and measure their sizes
  - "Thicken" up the branches and look for "loops"

Illustrations

- Play filtering brain video
- Play thicking brain video

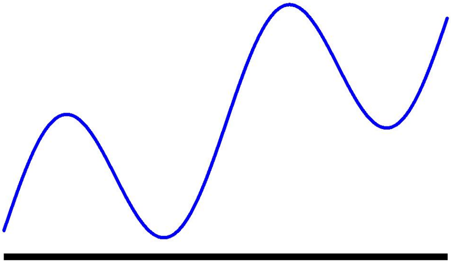
Persistence Diagrams

- For each bend we ask two questions:
  - When did we filter (ie, add in edges) enough to see a bend form? (birth time)
  - When did we filter enough to see the complete bend? (death time)

Persistence Diagrams

- For each bend we ask two questions:
  - When did we filter (ie, add in edges) enough to see a bend form? (birth time)
  - When did we filter enough to see the complete bend? (death time)
- Each bend is assigned a birth/death pair

Persistent Homology



$$\mathrm{Dim}(H_0(\mathbb{X})) = 0$$

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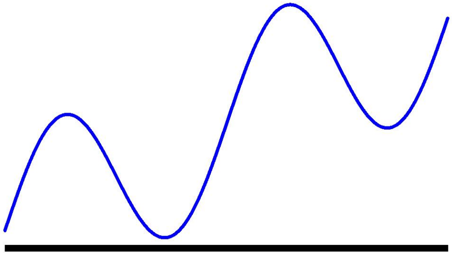

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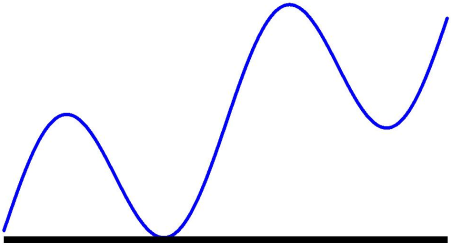

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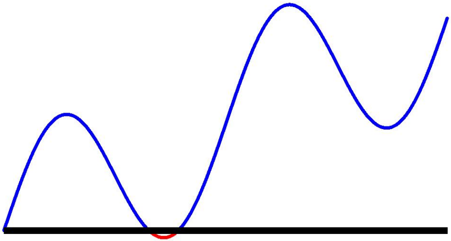

$$\text{Dim}(H_0(\mathbb{X})) = 1$$

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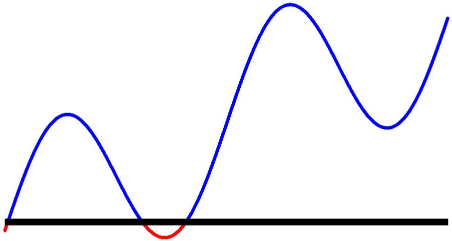

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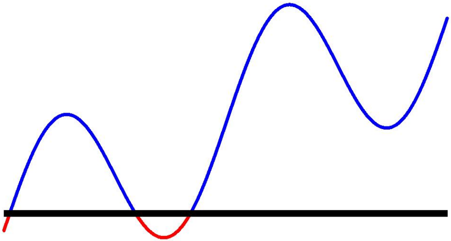

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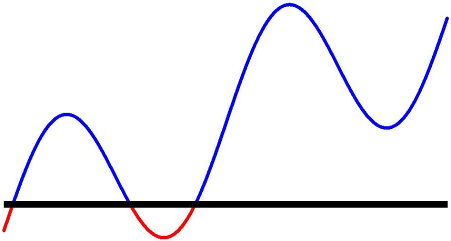

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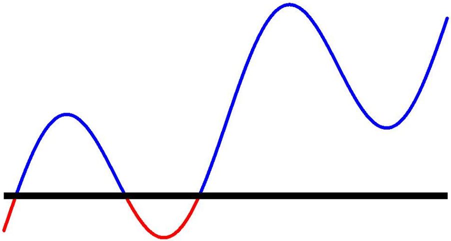

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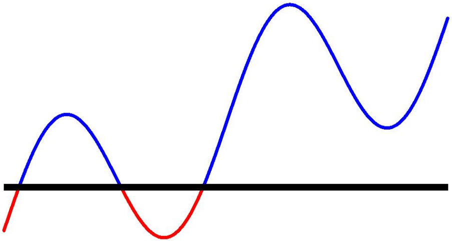

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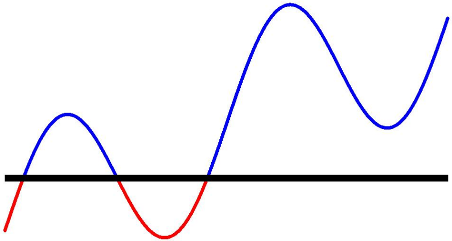

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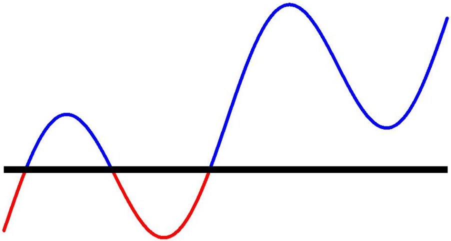

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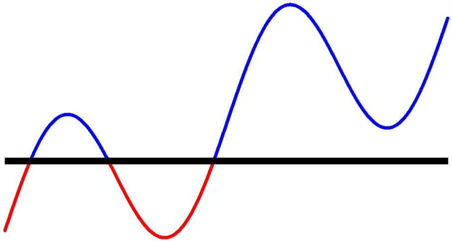
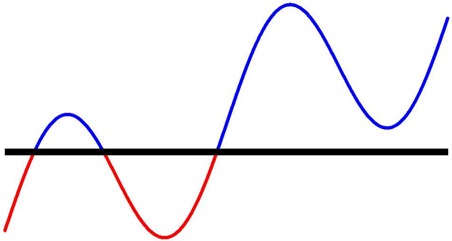
Persistent Homology



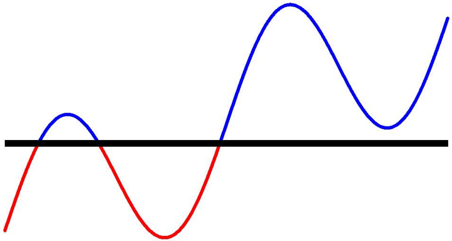
$$\mathrm{Dim}(H_0(\mathbb{X})) = 2$$

Persistent Homology



$$\mathrm{Dim}(H_0(\mathbb{X})) = 2$$

Persistent Homology



$$\mathrm{Dim}(H_0(\mathbb{X})) = 2$$

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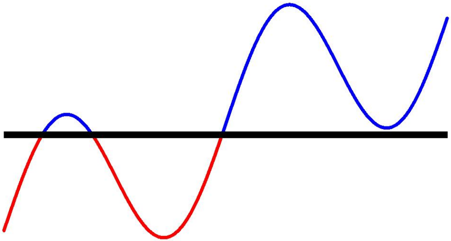
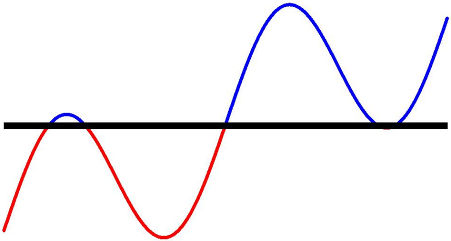


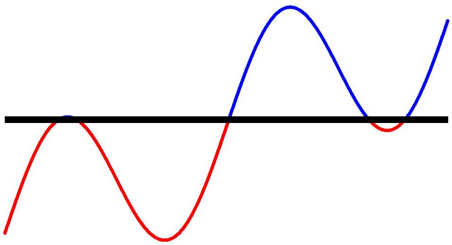
$$\mathrm{Dim}(H_0(\mathbb{X})) = 2$$

Persistent Homology



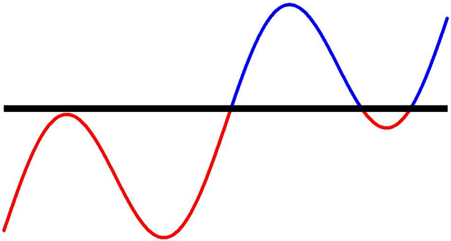
$$\mathrm{Dim}(H_0(\mathbb{X})) = 3$$

Persistent Homology



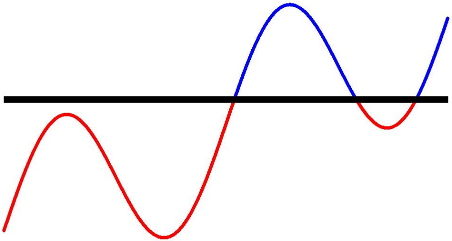
$\mathrm{Dim}(H_0(\mathbb{X})) = 3$

Persistent Homology



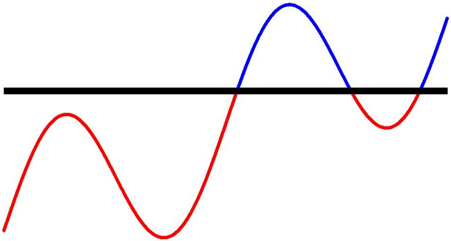
$$\mathrm{Dim}(H_0(\mathbb{X})) = 2$$

Persistent Homology



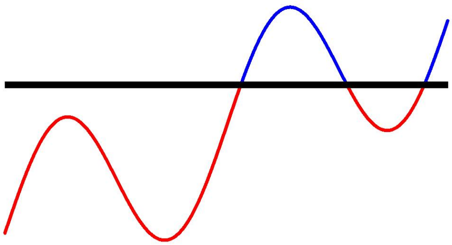
$$\mathrm{Dim}(H_0(\mathbb{X})) = 2$$

Persistent Homology



$$\mathrm{Dim}(H_0(\mathbb{X})) = 2$$

Persistent Homology



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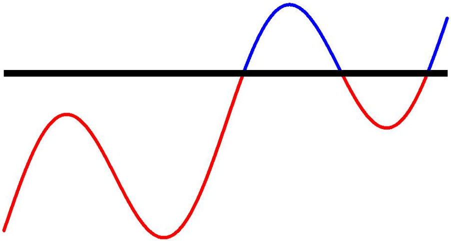
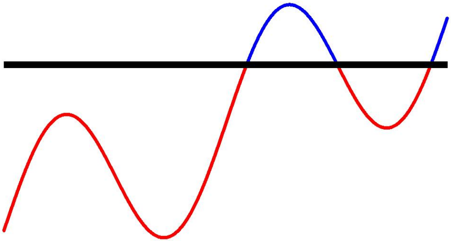
Persistent Homology



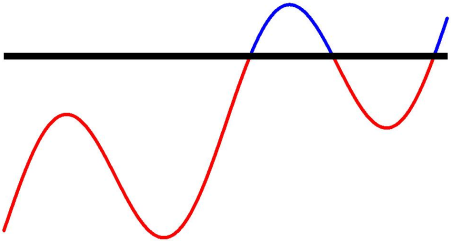
$$\text{Dim}(H_0(\mathbb{X})) = 2$$

Persistent Homology



$$\mathrm{Dim}(H_0(\mathbb{X})) = 2$$

Persistent Homology



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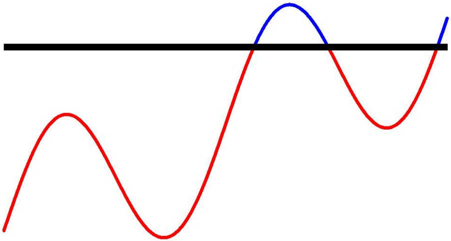
Persistent Homology



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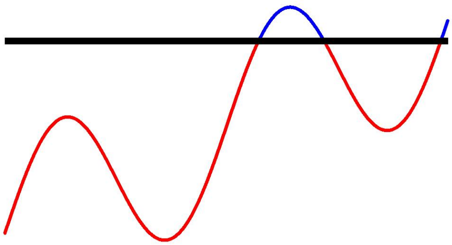

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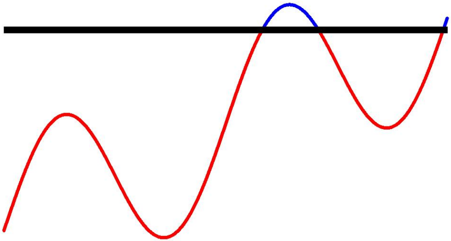

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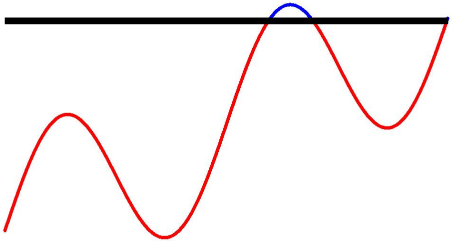
Persistent Homology



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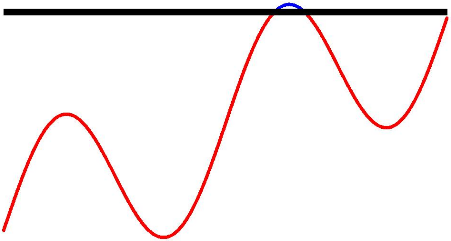
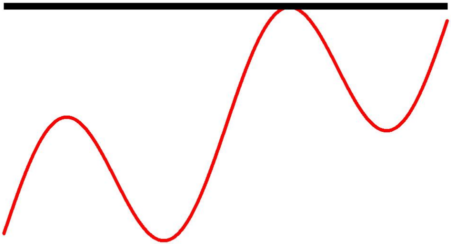
Persistent Homology



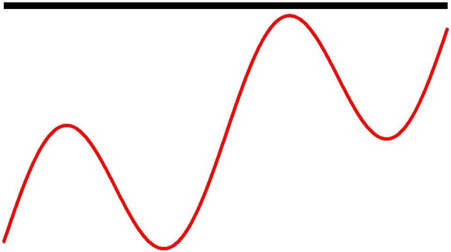
$$\text{Dim}(H_0(\mathbb{X})) = 2$$

Persistent Homology



$$\mathrm{Dim}(H_0(\mathbb{X})) = 2$$

Persistent Homology



$$\mathrm{Dim}(H_0(\mathbb{X})) = 1$$

Persistence Diagrams

- For each bend we ask two questions:
  - When did we filter (ie, add in edges) enough to see a bend form? (birth time)
  - When did we filter enough to see the complete bend? (death time)

Persistence Diagrams

- For each bend we ask two questions:
  - When did we filter (ie, add in edges) enough to see a bend form? (birth time)
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- For each bend we ask two questions:
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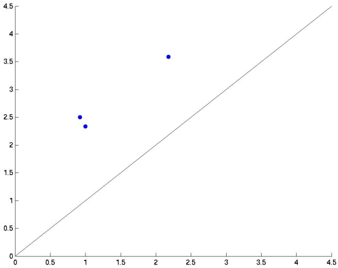
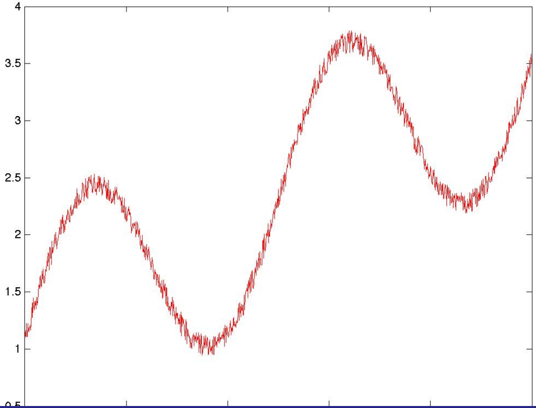
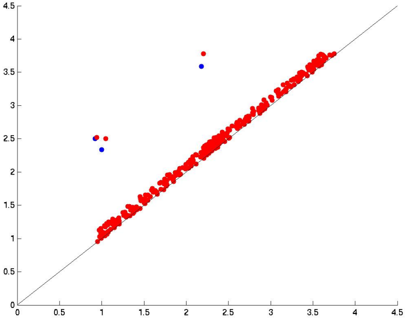


Stability of Persistent Homology

To what extent are persistence diagrams stable under addition of noise?

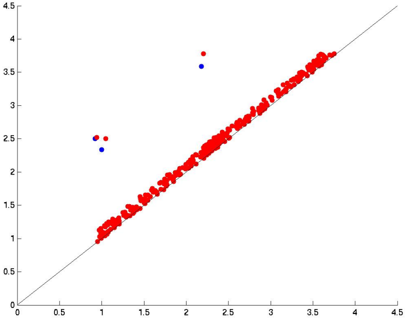


Stability of Persistent Homology



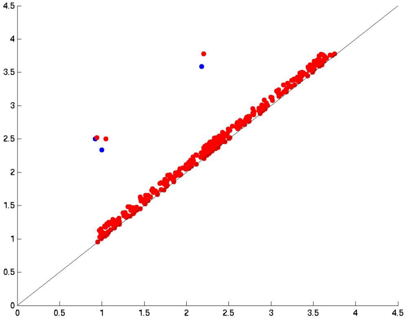
Stability of Persistent Homology

- Robust to changes in the initial topological space



Stability of Persistent Homology

- Robust to changes in the initial topological space
- If we “wiggle” original space by some ϵ, then persistence diagrams will only change by an ϵ



Persistence Diagrams

- For each “loop” we ask two questions:
  - When did we “thicken” the tree enough for loop to form? (birth time)
  - When did we “thicken” the tree enough for loop to fill in? (death time)

Persistence Diagrams

- For each “loop” we ask two questions:
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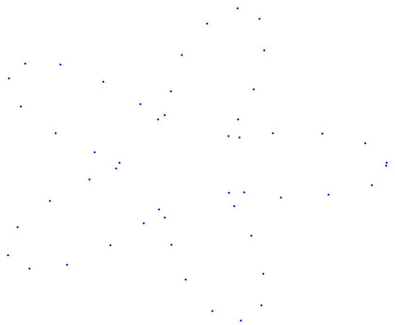
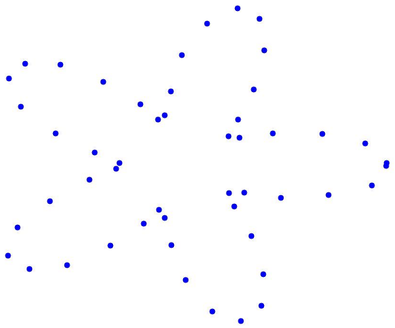
Persistent Homology



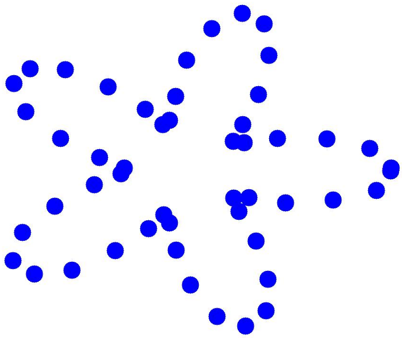
$\text{Dim}(H_0(\mathbb{X})) = 50 \qquad \text{Dim}(H_1(\mathbb{X})) = 0$

Persistent Homology



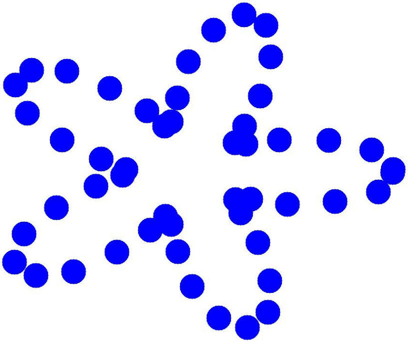
$$\text{Dim}(H_0(\mathbb{X})) = 49 \qquad \text{Dim}(H_1(\mathbb{X})) = 0$$

Persistent Homology



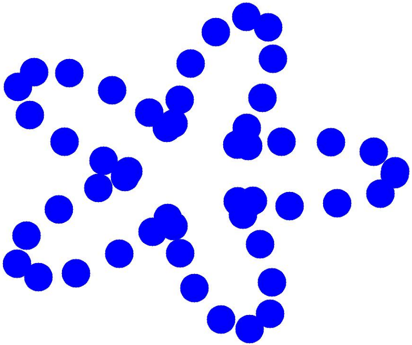
$\text{Dim}(H_0(\mathbb{X})) = 43 \qquad \text{Dim}(H_1(\mathbb{X})) = 1$

Persistent Homology



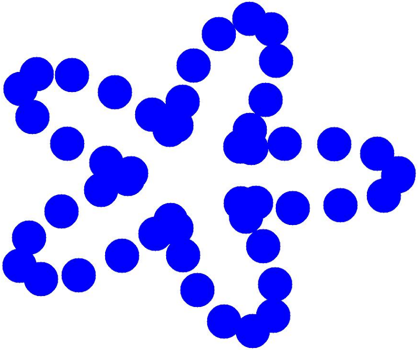
$$\text{Dim}(H_0(\mathbb{X})) = 36 \qquad \text{Dim}(H_1(\mathbb{X})) = 0$$

Persistent Homology



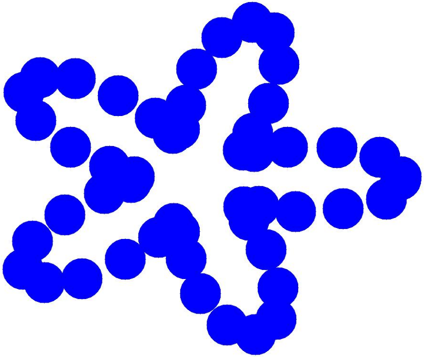
$\mathrm{Dim}(H_0(\mathbb{X})) = 31 \qquad \mathrm{Dim}(H_1(\mathbb{X})) = 1$

Persistent Homology



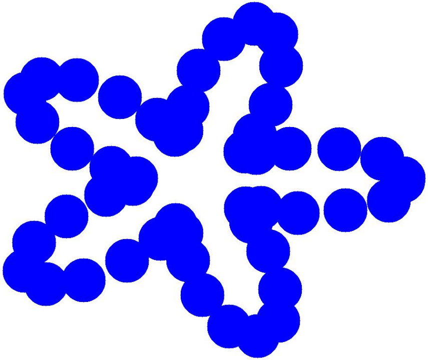
$\text{Dim}(H_0(\mathbb{X})) = 21 \qquad \text{Dim}(H_1(\mathbb{X})) = 0$

Persistent Homology



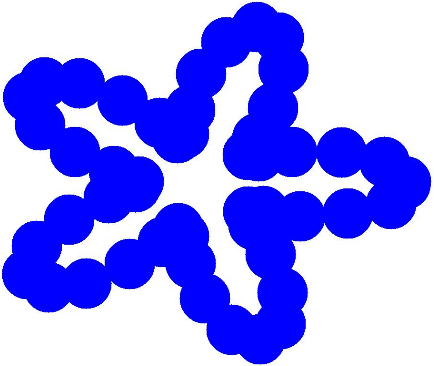
$\mathrm{Dim}(H_0(\mathbb{X})) = 12 \qquad \mathrm{Dim}(H_1(\mathbb{X})) = 0$

Persistent Homology



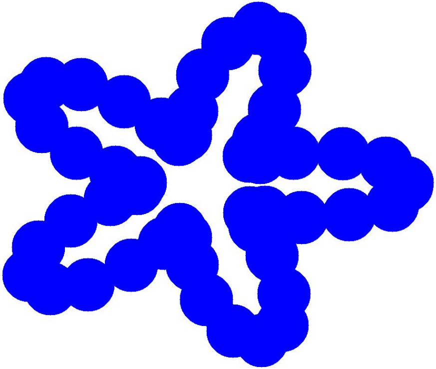
$\mathrm{Dim}(H_0(\mathbb{X})) = 7$ $\mathrm{Dim}(H_1(\mathbb{X})) = 0$

Persistent Homology



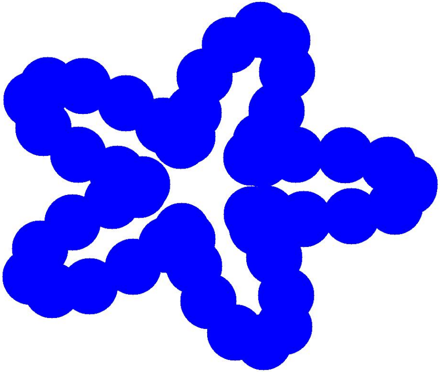
$\text{Dim}(H_0(\mathbb{X})) = 1$ $\text{Dim}(H_1(\mathbb{X})) = 1$

Persistent Homology



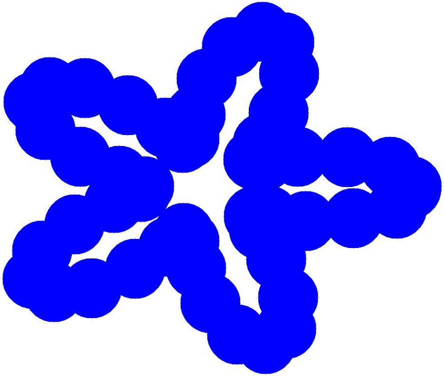
$\text{Dim}(H_0(\mathbb{X})) = 1$ $\text{Dim}(H_1(\mathbb{X})) = 1$

Persistent Homology



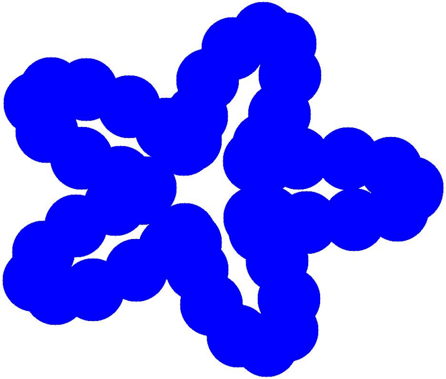
$\text{Dim}(H_0(\mathbb{X})) = 1 \qquad \text{Dim}(H_1(\mathbb{X})) = 2$

Persistent Homology



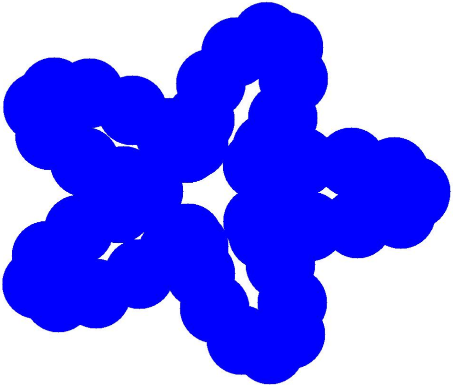
$\mathrm{Dim}(H_0(\mathbb{X})) = 1$ $\mathrm{Dim}(H_1(\mathbb{X})) = 4$

Persistent Homology



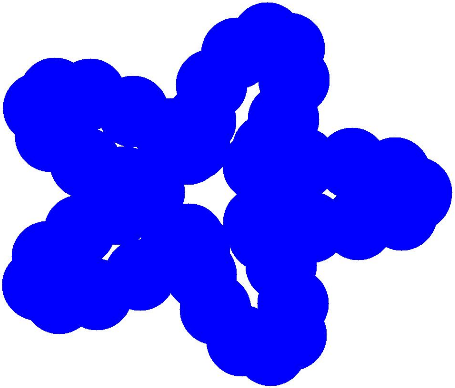
$\text{Dim}(H_0(\mathbb{X})) = 1$ $\text{Dim}(H_1(\mathbb{X})) = 5$

Persistent Homology



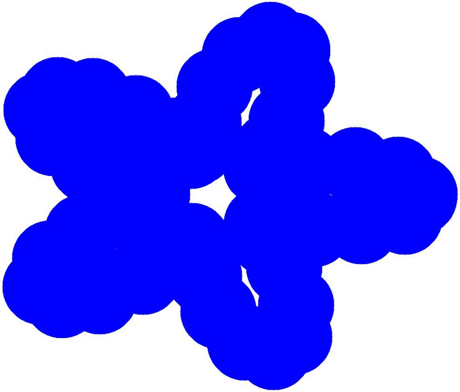
$\text{Dim}(H_0(\mathbb{X})) = 1 \qquad \text{Dim}(H_1(\mathbb{X})) = 7$

Persistent Homology



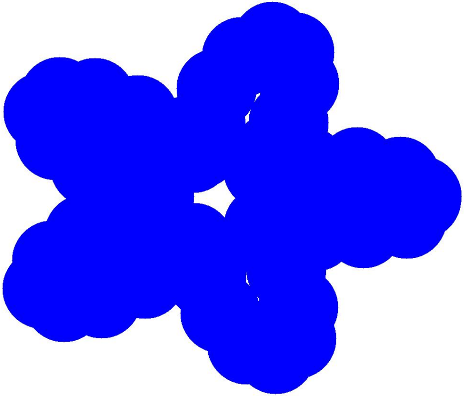
$\mathrm{Dim}(H_0(\mathbb{X})) = 1$ $\mathrm{Dim}(H_1(\mathbb{X})) = 9$

Persistent Homology



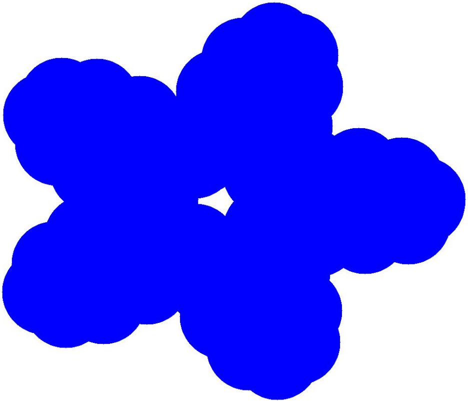
$\mathrm{Dim}(H_0(\mathbb{X})) = 1 \qquad \mathrm{Dim}(H_1(\mathbb{X})) = 3$

Persistent Homology



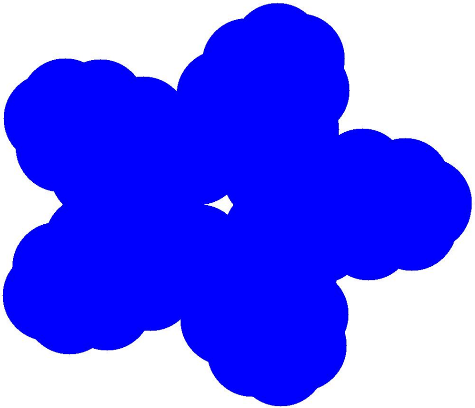
$\mathrm{Dim}(H_0(\mathbb{X})) = 1$ $\mathrm{Dim}(H_1(\mathbb{X})) = 5$

Persistent Homology



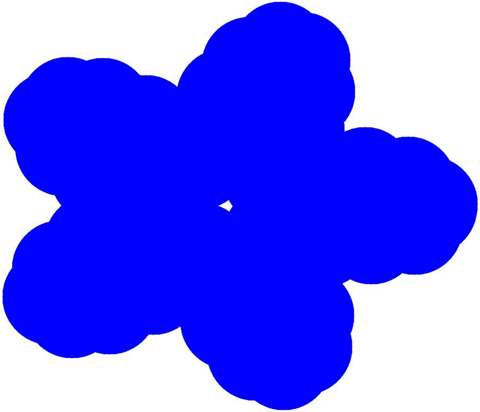
$\mathrm{Dim}(H_0(\mathbb{X})) = 1$ $\mathrm{Dim}(H_1(\mathbb{X})) = 1$

Persistent Homology



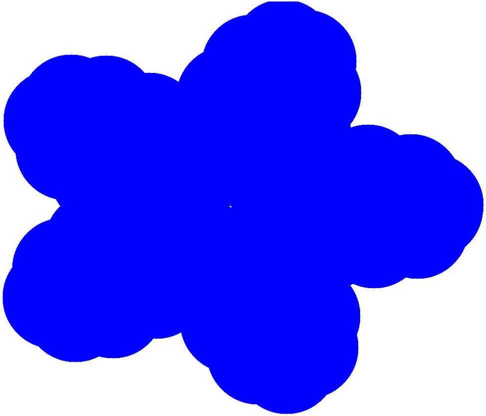
$\text{Dim}(H_0(\mathbb{X})) = 1$ $\text{Dim}(H_1(\mathbb{X})) = 1$

Persistent Homology



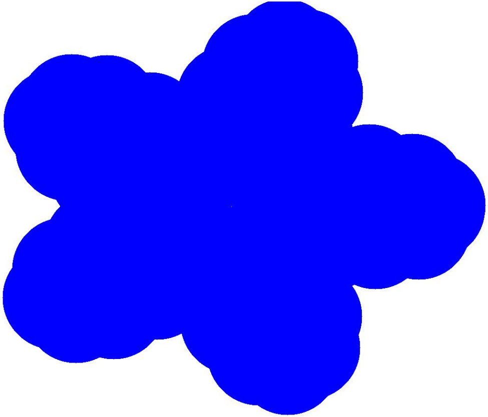
$\text{Dim}(H_0(\mathbb{X})) = 1$ $\text{Dim}(H_1(\mathbb{X})) = 1$

Persistent Homology



$\mathrm{Dim}(H_0(\mathbb{X})) = 1$ $\mathrm{Dim}(H_1(\mathbb{X})) = 1$

Persistent Homology



$\text{Dim}(H_0(\mathbb{X})) = 1 \qquad \text{Dim}(H_1(\mathbb{X})) = 0$

Persistence Diagrams

- For each “loop” we ask two questions:
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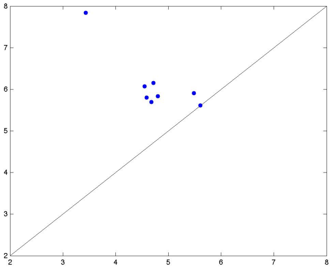

Goals

- Use Topological Data Analysis (TDA) and Persistent Homology to analyze the multi-scale geometry and topology of branching and looping structures in brain artery trees

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- Statistically analyze the 3D motifs that are identified by TDA in relation to covariates (age, sex, etc.)

Our Analysis and Results

3D Brain Tree → Persistence Diagrams → Feature Vectors

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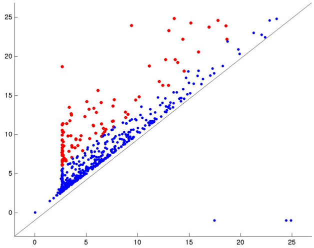
- Assign each point in the persistence diagram a persistence time (persistence time = death time − birth time)

Our Analysis and Results

3D Brain Tree → Persistence Diagrams → Feature Vectors

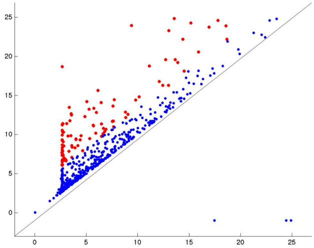
- Assign each point in the persistence diagram a persistence time (persistence time = death time — birth time)
- Look particularly at top 100 persistence times or top 100 persistence times points with their birth times



Our Analysis and Results

3D Brain Tree → Persistence Diagrams → Feature Vectors

- Assign each point in the persistence diagram a persistence time (persistence time = death time — birth time)
- Look particularly at top 100 persistence times or top 100 persistence times points with their birth times
- Defines a feature vector for each brain artery tree



Our Analysis and Results

3D Brain Tree → Persistence Diagrams → Feature Vectors

Dimensionality Reduction

Our Analysis and Results

3D Brain Tree → Persistence Diagrams → Feature Vectors

Dimensionality Reduction

- Run principle component analysis on feature vectors

Our Analysis and Results

3D Brain Tree → Persistence Diagrams → Feature Vectors

Dimensionality Reduction

- Run principle component analysis on feature vectors
- Find first principle component vector (PC1)

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3D Brain Tree → Persistence Diagrams → Feature Vectors

Dimensionality Reduction

- Run principle component analysis on feature vectors
- Find first principle component vector (PC1)
- Find each feature vector's length along PC1

Our Analysis and Results

3D Brain Tree → Persistence Diagrams → Feature Vectors

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Analyses

Our Analysis and Results

3D Brain Tree → Persistence Diagrams → Feature Vectors

Dimensionality Reduction

- Run principle component analysis on feature vectors
- Find first principle component vector (PC1)
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Analyses

- Age: Correlate the log of the PC1 lengths with respective ages

Our Analysis and Results

3D Brain Tree → Persistence Diagrams → Feature Vectors

Dimensionality Reduction

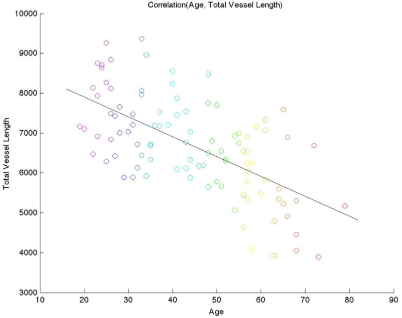
- Run principle component analysis on feature vectors
- Find first principle component vector (PC1)
- Find each feature vector's length along PC1

Analyses

- Age: Correlate the log of the PC1 lengths with respective ages
- Sex: Run a permutation test on the feature vectors of different sexes

Age vs Total Vessel Length

Pearson Correlation = **0.6243**
p-value = $\mathbf{6.46 \times 10^{-12}}$



Reproduced result from (Bullitt-Aylward, 2002)

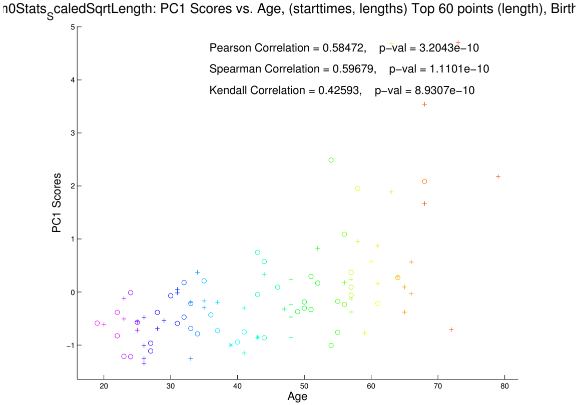
Scaling Feature Vectors

- Want to remove other confounding variables
- Scale our feature vectors to remove possible confounding variables

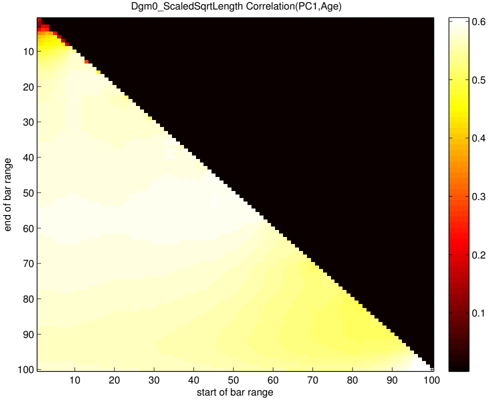
$$\frac{\text{Feature Vector}}{\sqrt{\text{Total Vessel Length}}}$$

Analysis of Age: 0-Dimensional

Pearson Correlation: **0.57**
p-value: $\mathbf{1.07 \times 10^{-9}}$

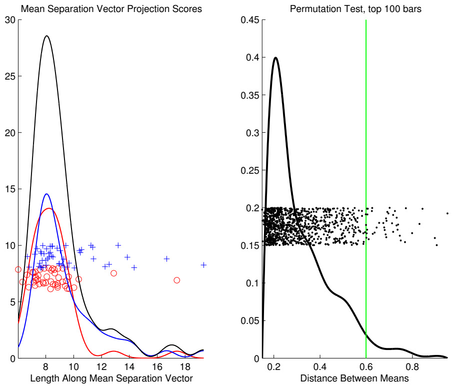


Analysis of Age: 0-Dimensional



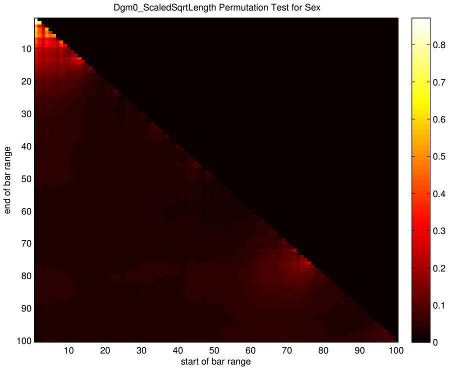
Analysis of Different Sexes: 0-Dimensional

Sex Difference *p*-value: **4.1%**



Analysis of Different Sexes: 0-Dimensional

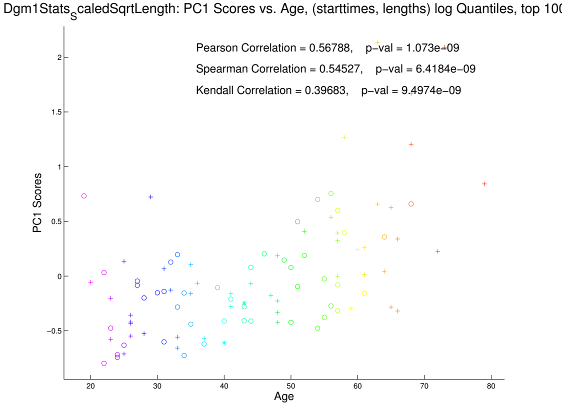
Sex Difference Mean p-value: **0.0485**
Sex Difference Std of p-value: **0.044**
Sex Difference Median p-value: **0.038**



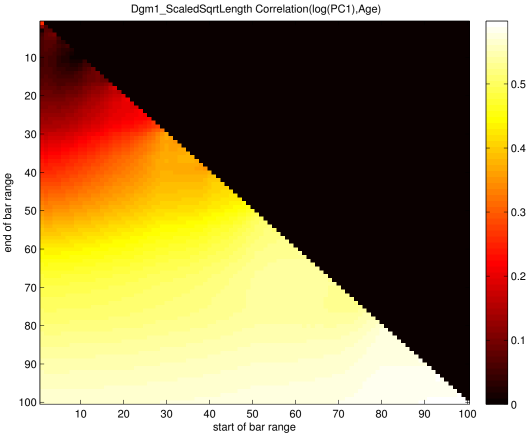
Analysis of Age: 1-Dimensional

Pearson Correlation: **0.5409**

p-value: $\mathbf{9.43 \times 10^{-9}}$

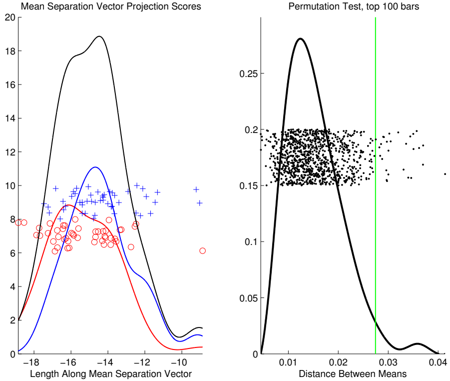


Analysis of Age: 1-Dimensional



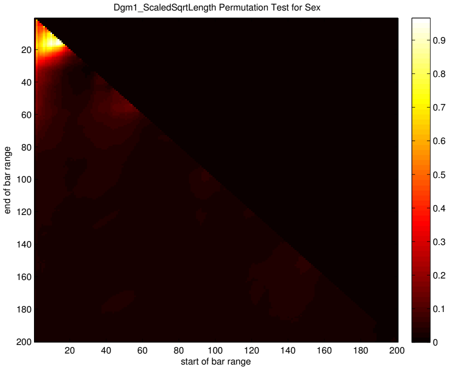
Analysis of Different Sexes: 1-Dimensional

Sex Difference *p*-value: **2.8%**



Analysis of Different Sexes: 1-Dimensional

Sex Difference Mean *p*-value: **0.0414**
Sex Difference Std of *p*-value: **0.0719**
Sex Difference Median *p*-value: **0.028**



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- High-persistence points correspond to big geometric features
- Small-persistence points correspond to small geometric features, but might be noise
- BUT, large persistence does not imply significant
- TDA and persistent homology can quantify and distinguish between geometric motifs in cerebrovascular system

Questions???