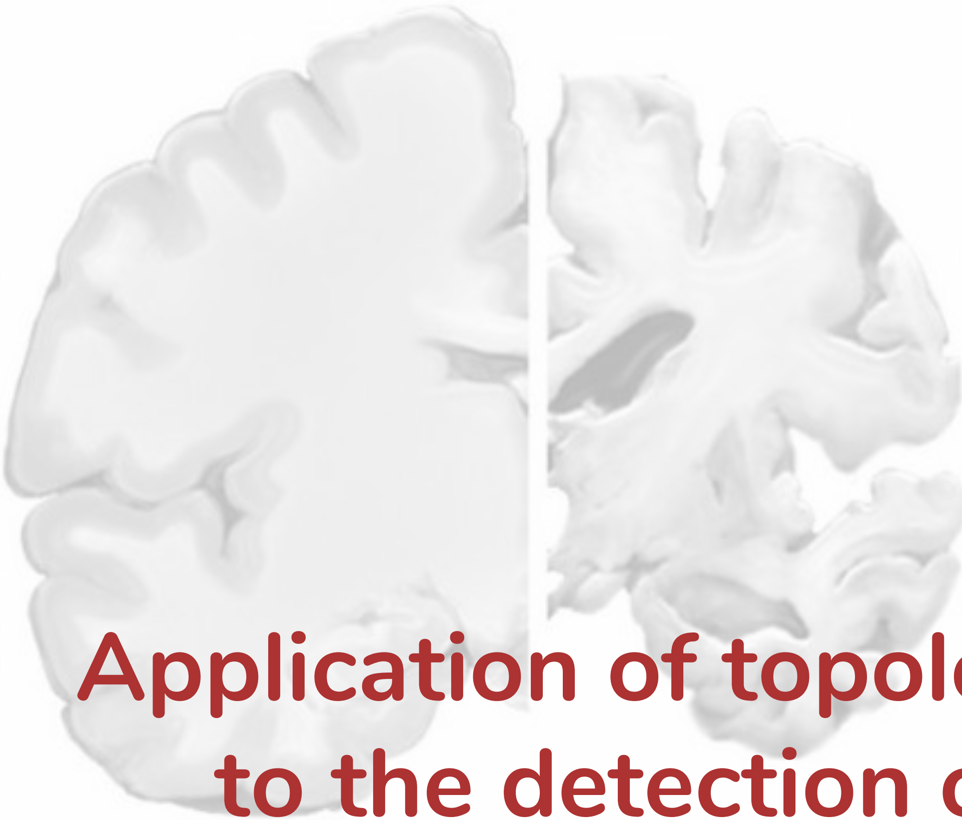

Application of topological data analysis to the detection of mild cognitive impairment

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Alzheimer’s Disease

Alzheimer's is a type of dementia that causes problems with memory, thinking and behavior.
Symptoms usually develop slowly and get worse over time, becoming severe enough to interfere with daily tasks.

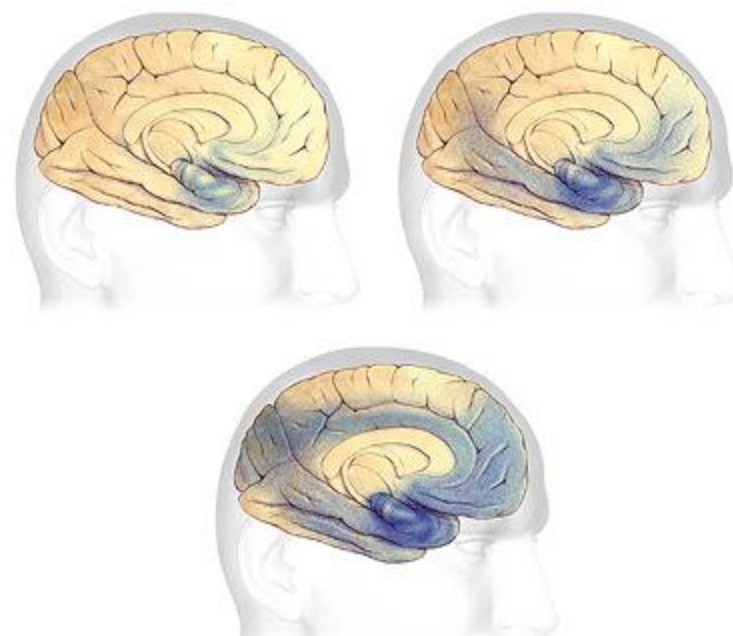
Two abnormal structures called plaques and tangles are prime suspects in damaging and killing nerve cells.

Plaques are deposits of beta-amyloid that build up in the spaces between nerve cells

Tangles are twisted fibers of another protein called tau that build up inside cells

In the mildly symptomatic stages, pathological brain atrophy can be subtle and overpowered due to signal by aging.

Our aim: Predict cognitive status using topological features of brain atrophy that are indicative of mild cognitive impairment.



ImaGene study

155 participants:
- 105 mild cognitive impairment (MCI)
  - Amnestic MCI (aMCI)
  - Non-amnestic MCI (naMCI)
- 50 cognitively normal (CN) individuals (at Base Line)

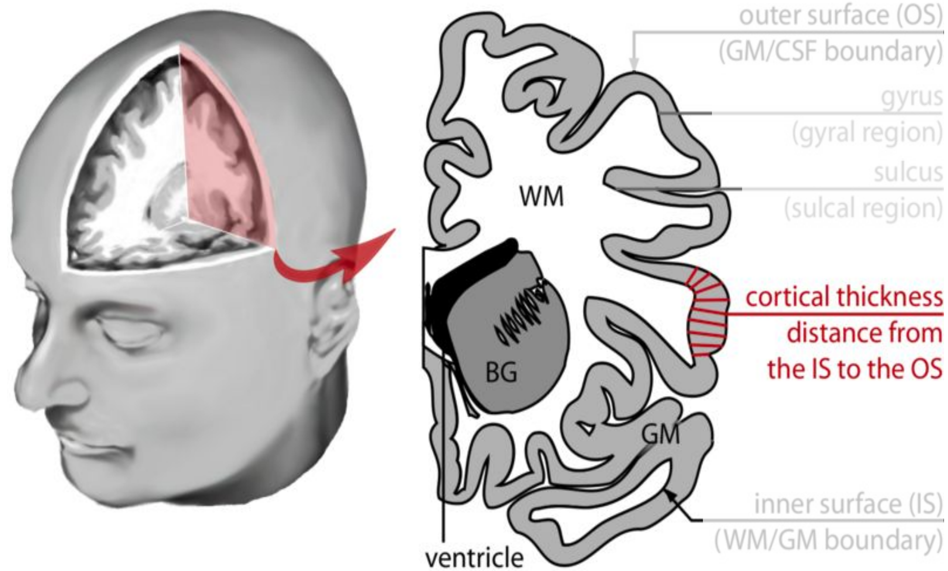
All participants' condition was assessed annually over 5 years.

Clinical measures, cognitive measures, structural imaging, Amyloid PET, genetic & epigenetic data, plasma and serum.

Variable	NC (N=52)	aMCI (N=69)	naMCI (N=38)	P-value
Age, yr	69.03 (7.9)	69.28 (8.5)	69.78 (8.5)	0.9
Education, yr	17.6 (2.04)	15.5 (2.7)	16.5 (2.88)	0.001
Gender, M/F	30/21	26/43	20/18	

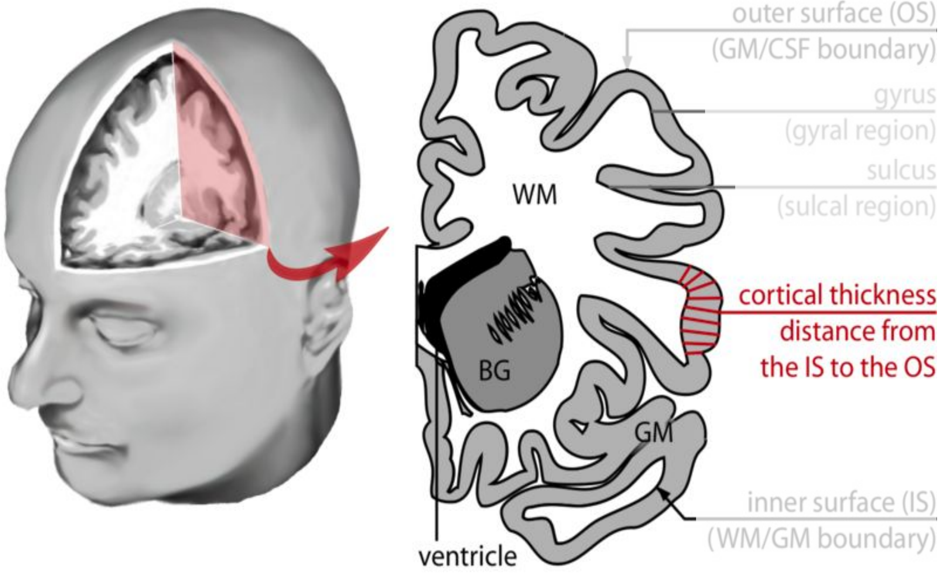
Cortical thickness

Healthy **Severe AD**



Cortical thickness

Structural imaging

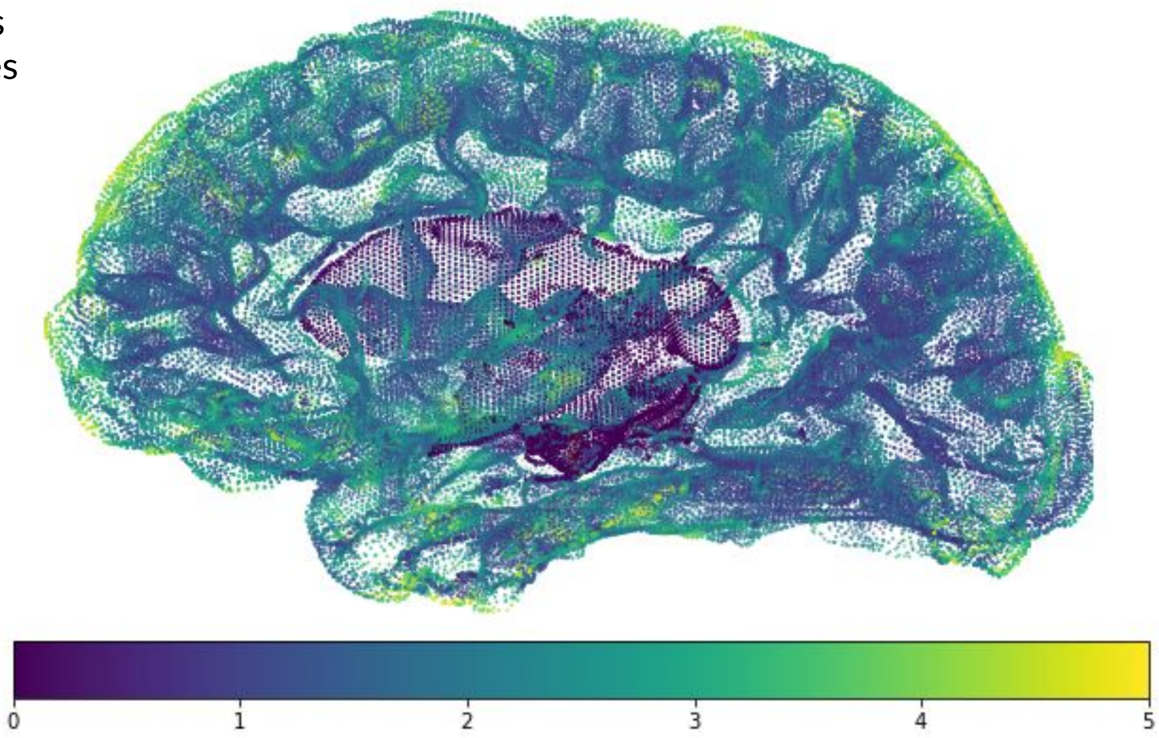


Brain meshes

Cortical thickness brain meshes were derived using FreeSurfer 6.0.0. (vertex-wise regressions across all subjects). Age was additionally regressed out of the thickness data.

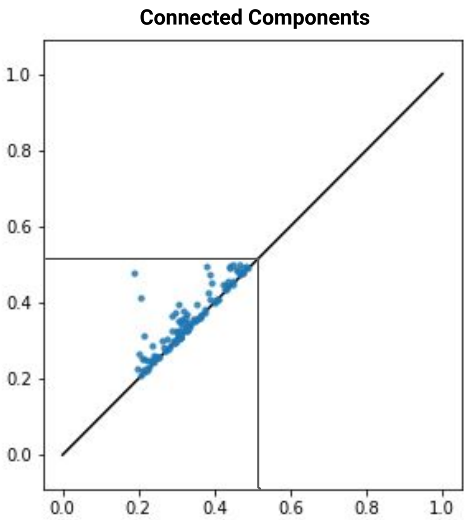
Constructed meshes:

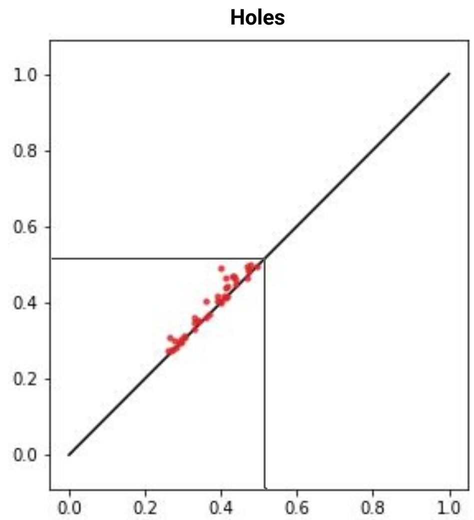
- 327684 Vertices
- 655360 Triangles

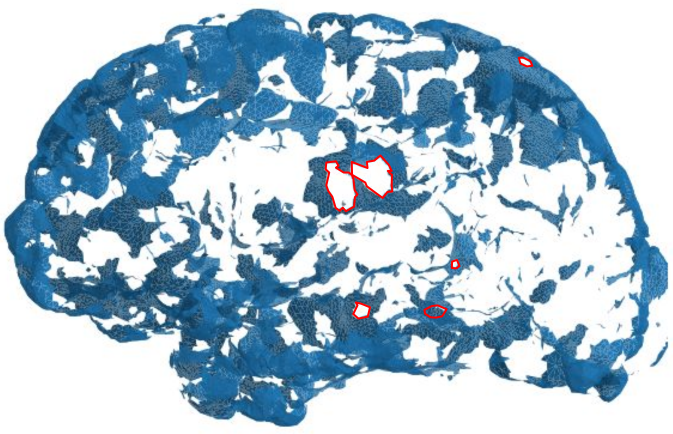


Brain meshes

Objective: Use cortical thickness to build a coarse descriptor of the surface that still retains meaningful information about the data set.







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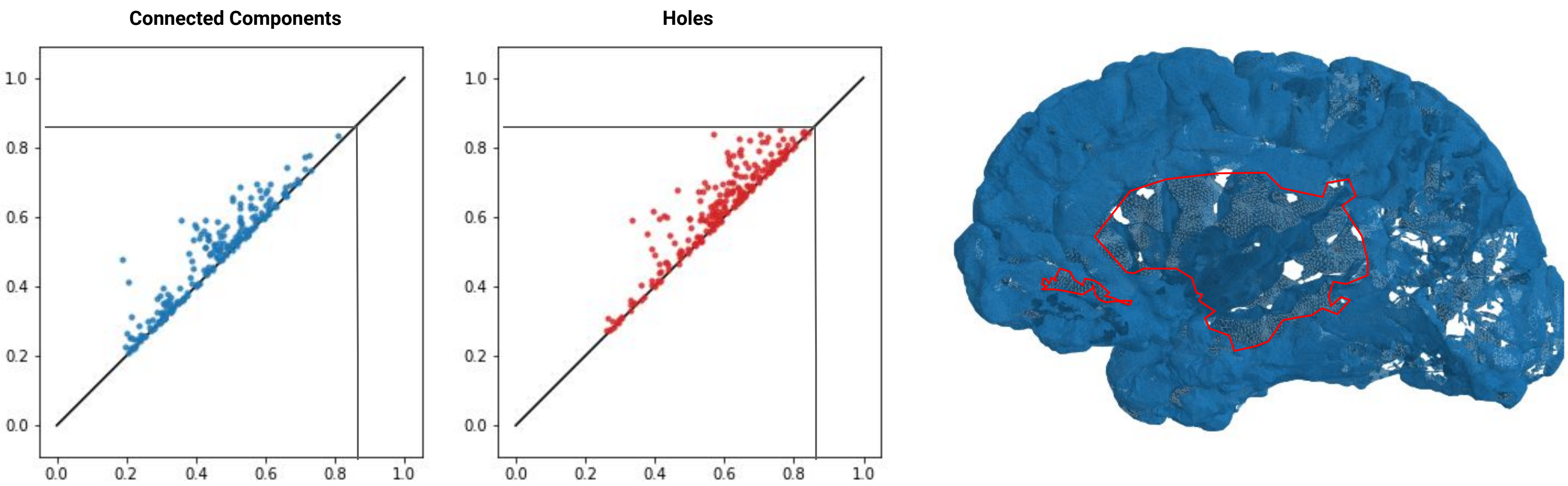

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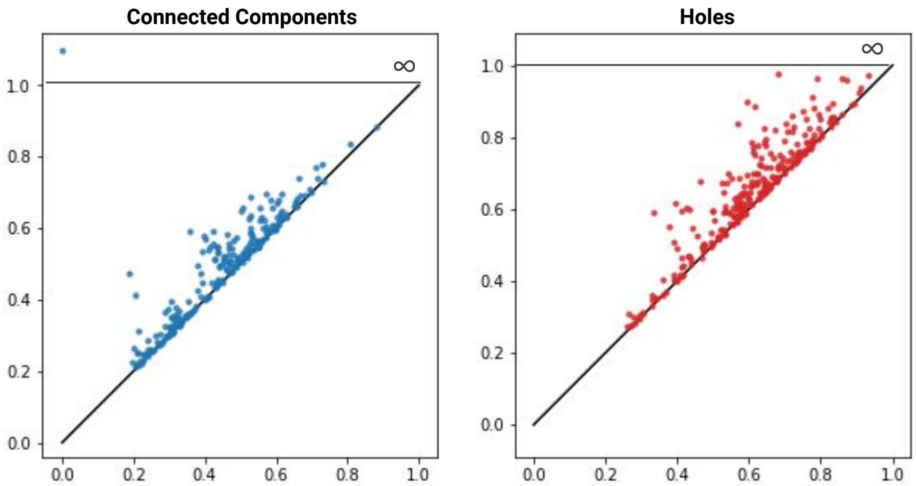
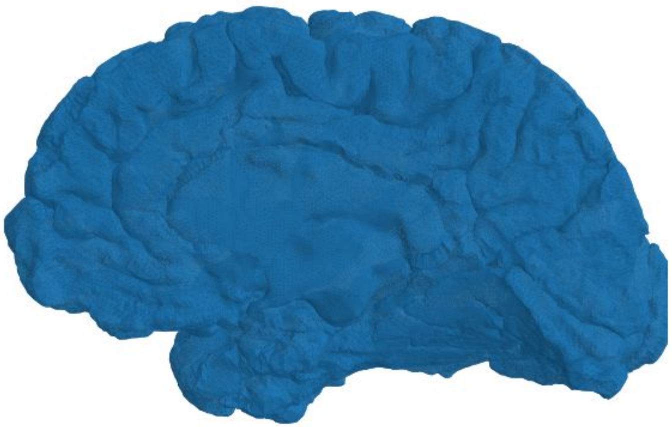


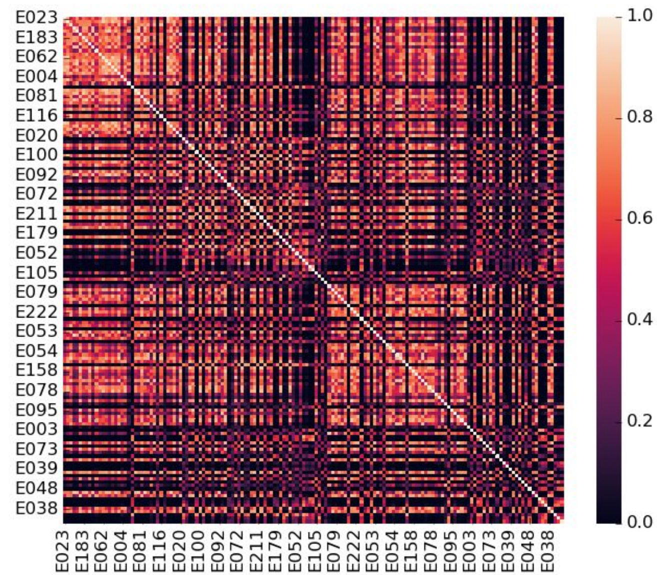


The persistent scale-space kernel

Persistent scale-space kernel intuition:
To build the map to an Hilbert space, each persistence diagram D can be uniquely represented as a sum of Dirac delta distributions, one for each point in D.

$$k_\sigma(F,G) = \frac{1}{8\pi\sigma} \sum_{\substack{p\in F\\ q\in G}} e^{-\frac{\|p-q\|^2}{8\sigma}} - e^{-\frac{\|p-\bar{q}\|^2}{8\sigma}}$$

Sex and age



Build suitable kernels (quantify dissimilarity) from homological features

A Stable Multi-Scale Kernel for Topological Machine Learning. Reininghaus, Huber, Bauer & Kwitt 2015
Integrating Tara Oceans data sets using a multiple kernel approach. Mariette, et. al. (2016)

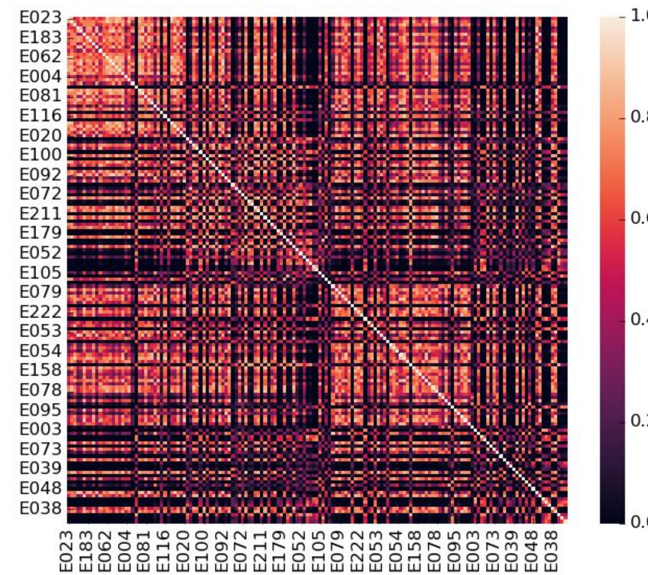
The persistent scale-space kernel

Following (Reininghaus et al. 2015) we build a persistent kernel from the persistence diagrams of dimension 0 and 1.

These kernels were combined using a **sparse-consensus-integration** approach introduced by (Mariette et al. 2016). The resulting kernel is a linear combination of the persistent scale-space kernels with coefficients:

$$C_{mm'} = \frac{\langle K^m, K^{m'} \rangle_F}{\|K^m\|_F \|K^{m'}\|_F} = \frac{\mathrm{Trace}(K^m K^{m'})}{\sqrt{\mathrm{Trace}((K^m)^2)\mathrm{Trace}((K^{m'})^2)}}.$$

Sex and age



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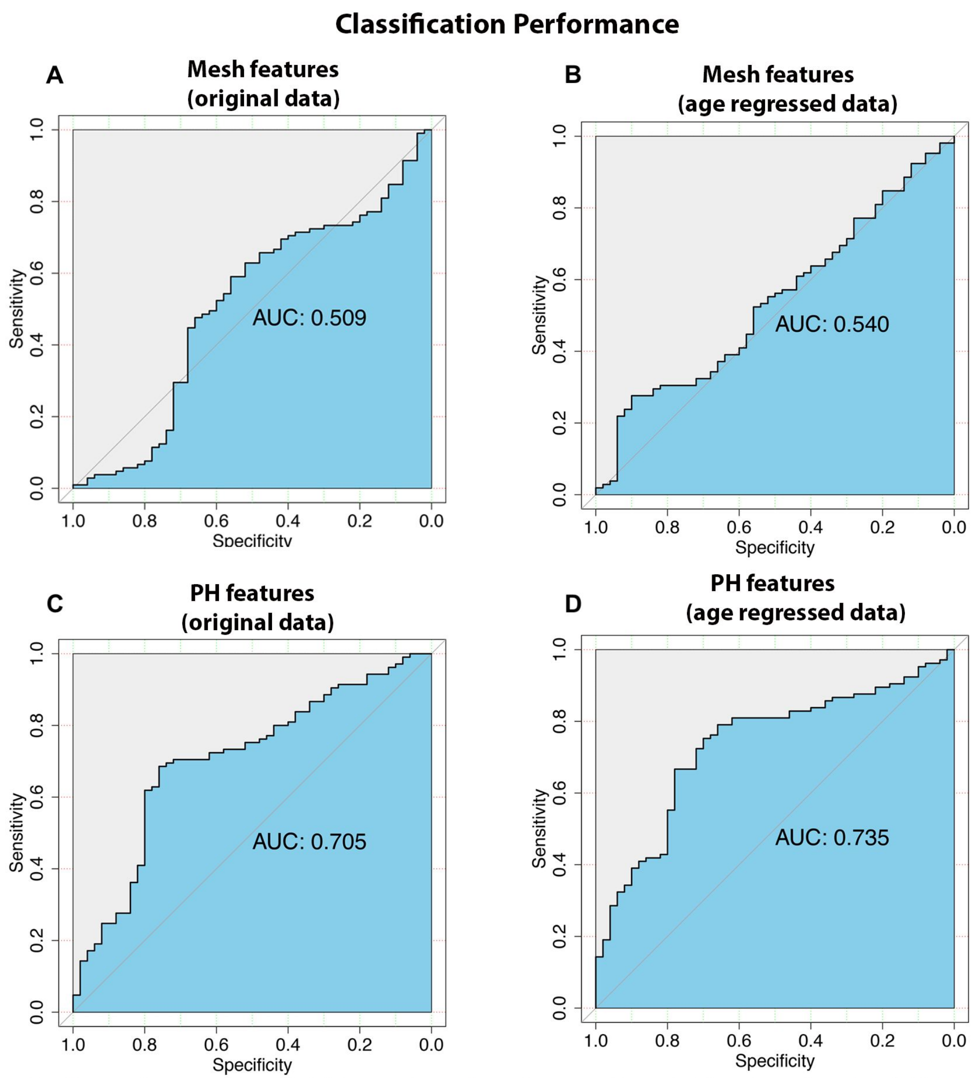
Supervised learning for subject classification

To validate the use of homological features, three demographic kernels were created for age, gender and education using Gaussian-radial-basis functions.

We trained four support vector machine classifiers, two for uncorrected data (homological-vs-mesh) and two for age-regressed data (homological-vs-mesh). Validation was done using a leave-one-out approach.

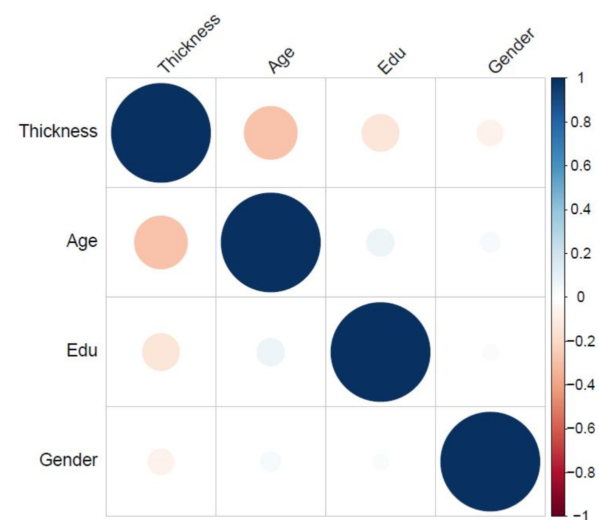
Supervised learning for subject classification



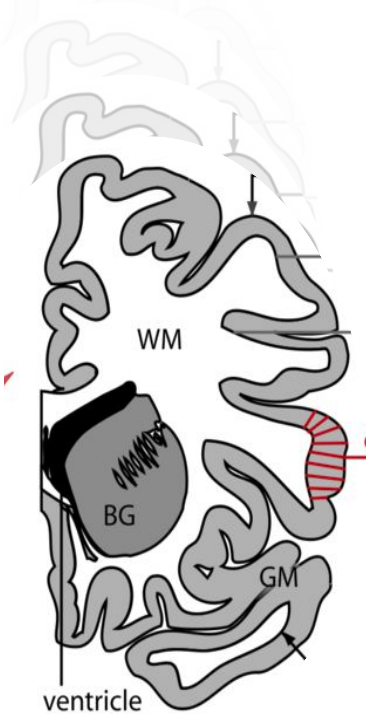
Top-Bottom: integrated kernel with free surfer meshes vs integrated kernel with peristant homology(PH) features
Left-Right: original vs age regressed data.

Similarity = True Positive Ratio

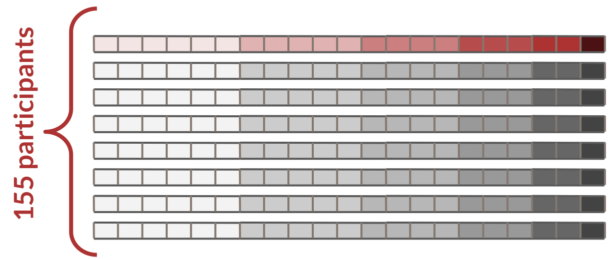
Specificity = False Positive Ratio



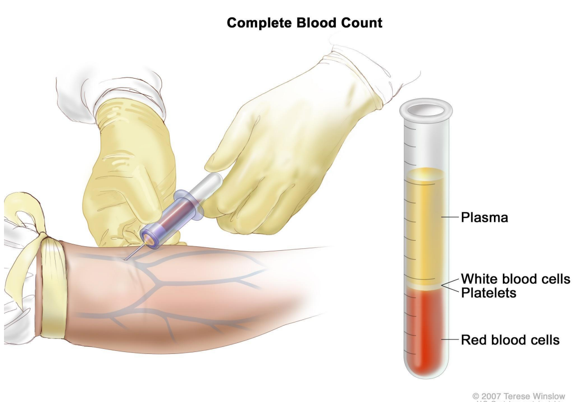
Work in progress

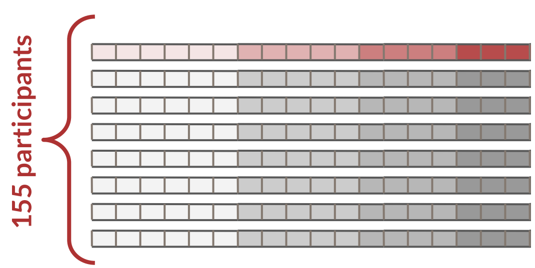


327684 vertices thickness

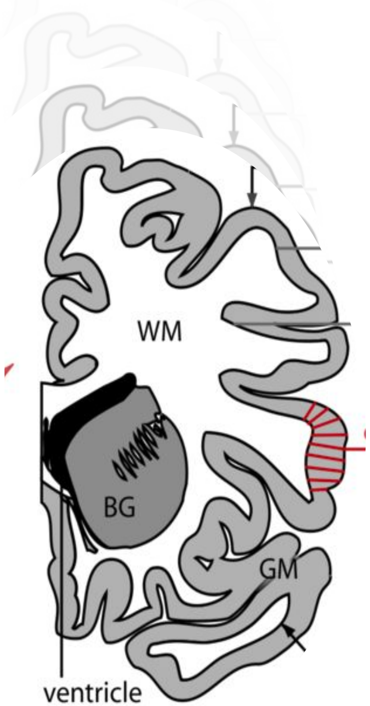


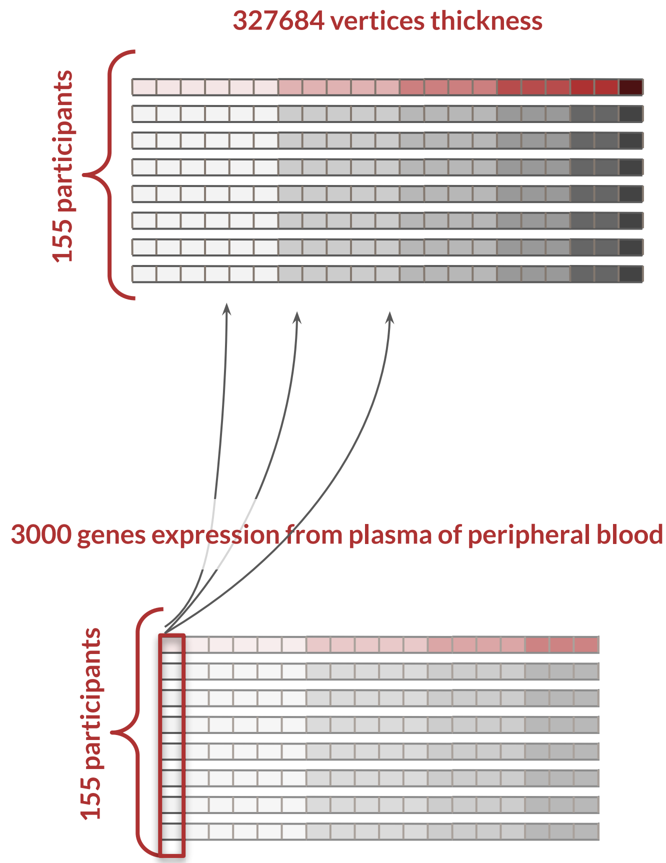
3000 genes expression from plasma of peripheral blood



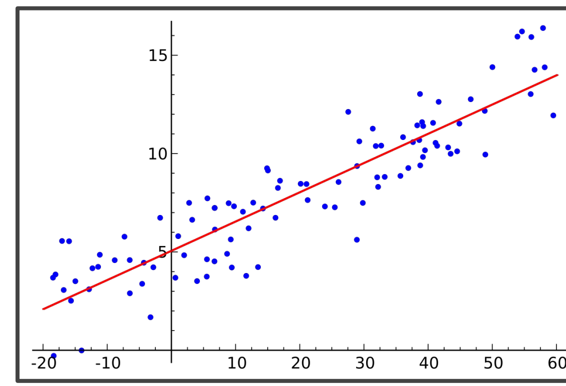


Work in progress - Adding genetic features

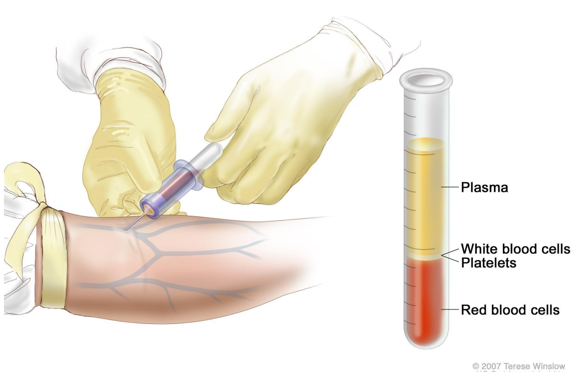




Linear Regression between vertex thickness across participants and gene-expression



*Sample image not actual data



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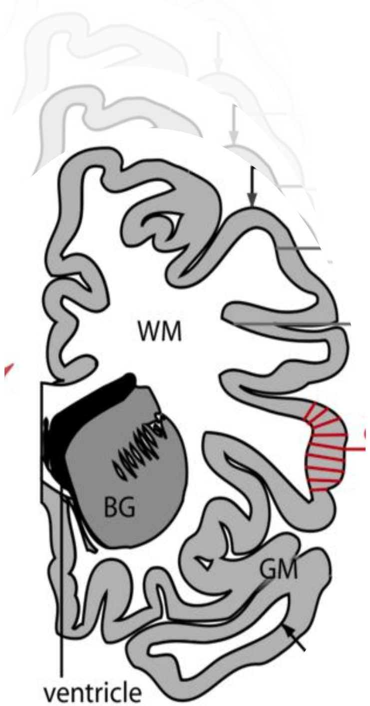
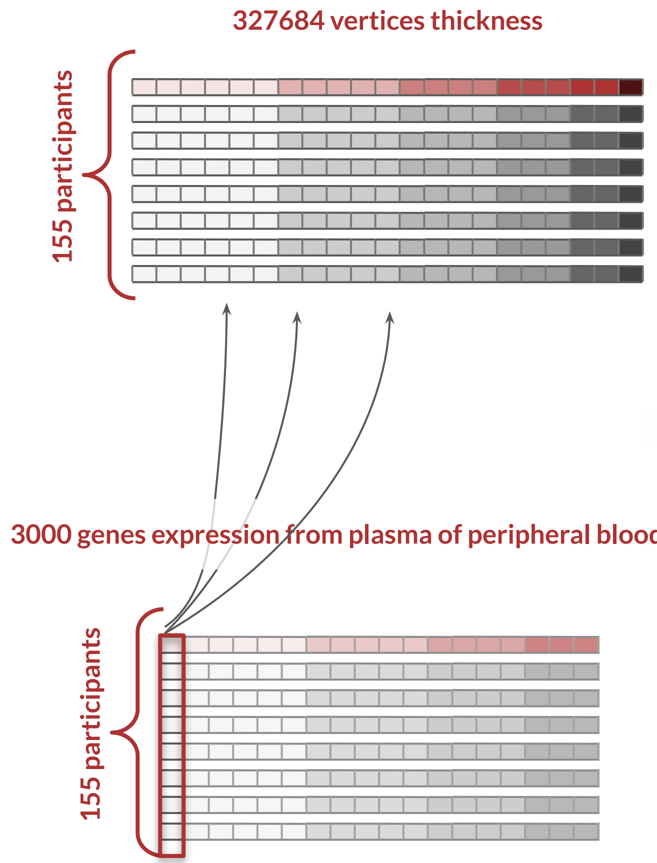
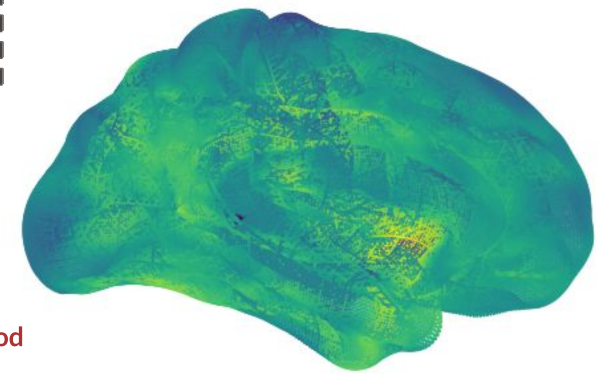
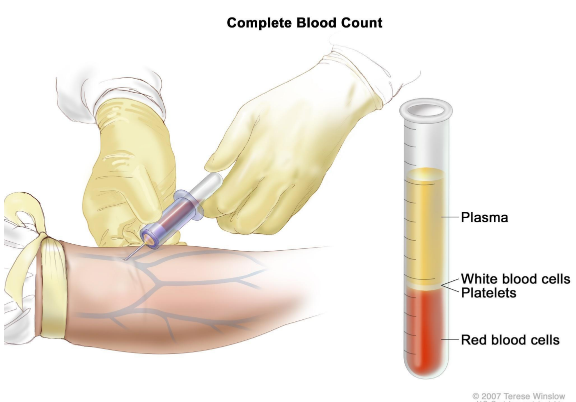




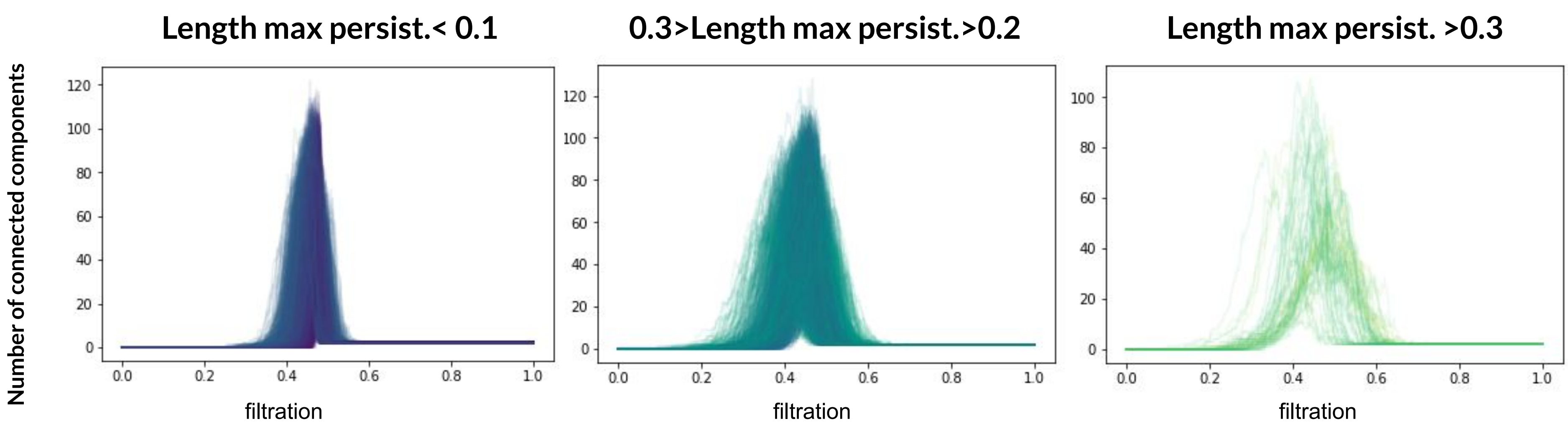
Beta coefficients of regression analysis for gene 1



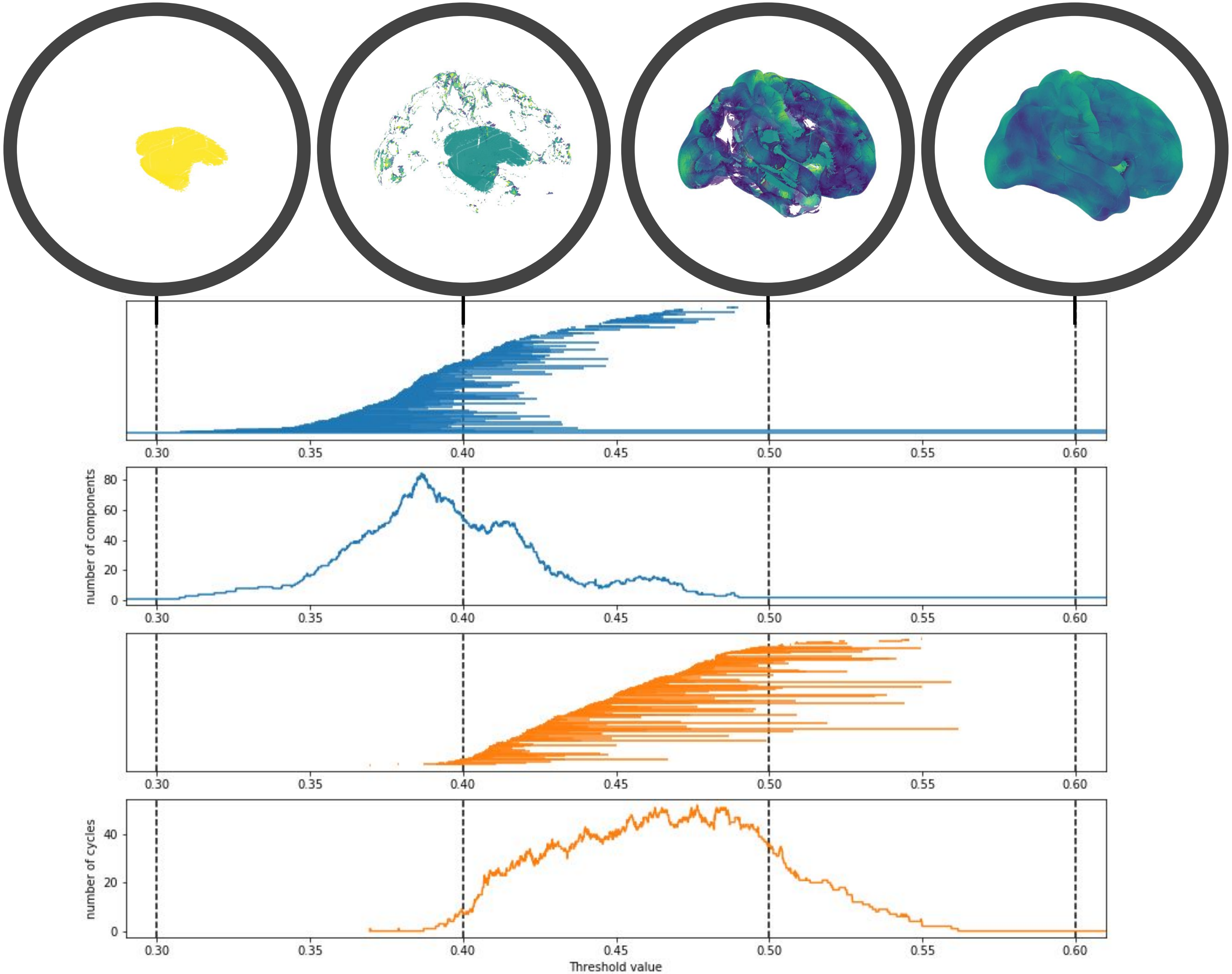


Connected components

Study of 3000 genes

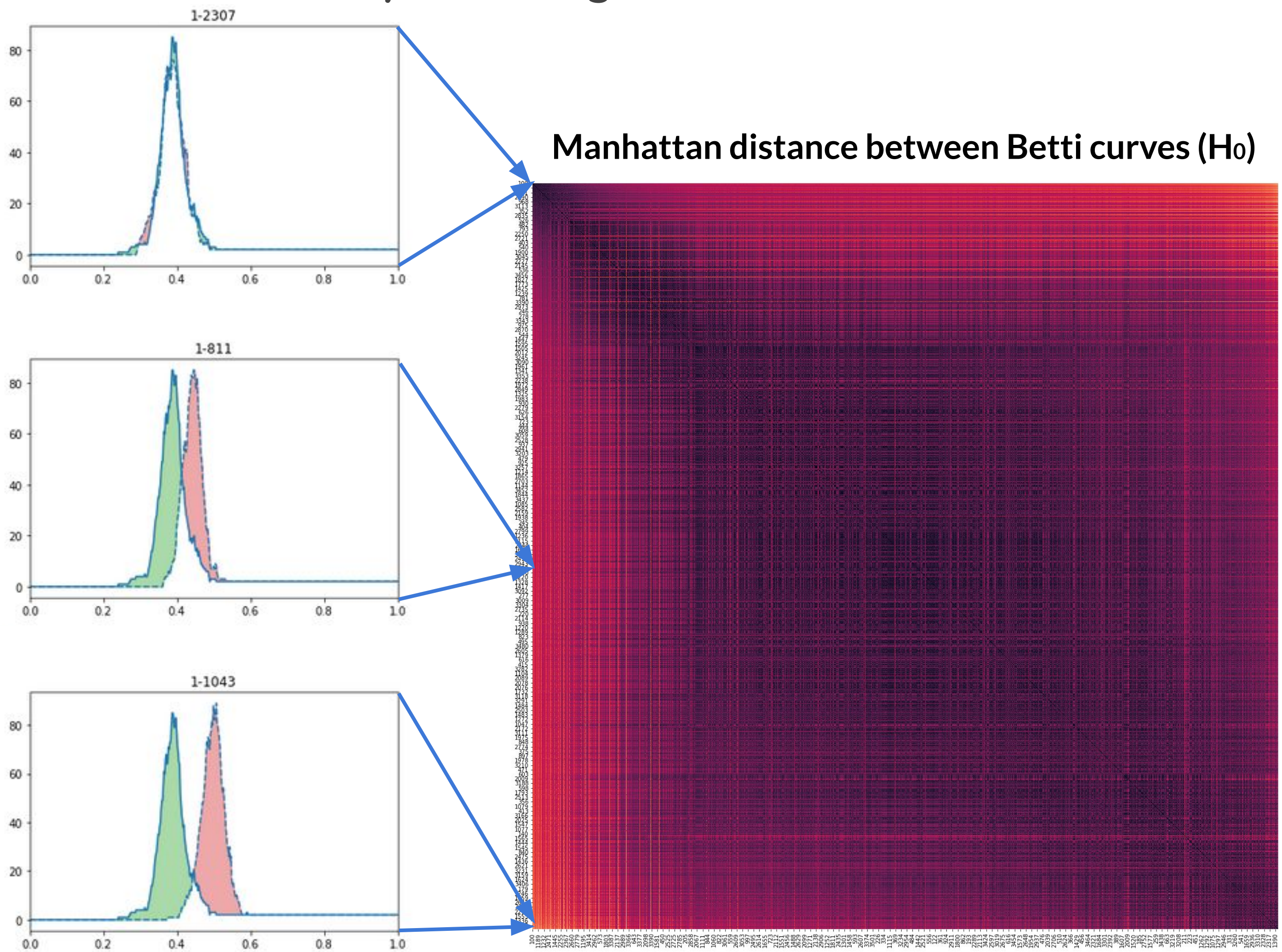


Persistent Homology



Connected components

Study of 3000 genes



Connected components

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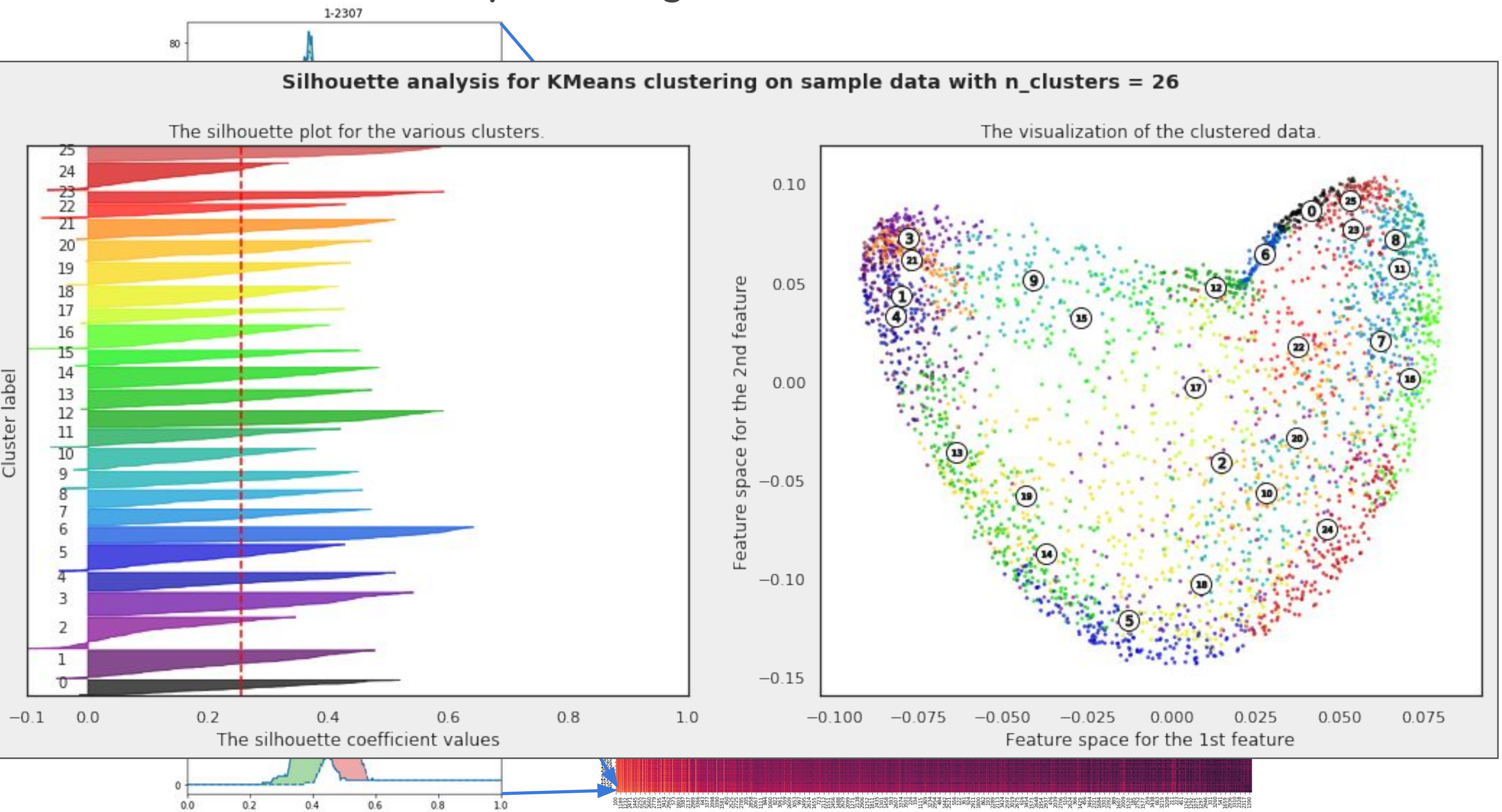

NIH NIA

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Thank you for the attention

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