



University of Wisconsin
SCHOOL OF MEDICINE
AND PUBLIC HEALTH

Topological State-Space Estimation of Dynamically Changing Functional Brain Networks

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Vince D. Calhoun **TRenDs, Georgia State, Georgia Tech,**
Emory State University, Georgia

Grants: NIH U01NS093650, NS117568, EB022856, EB028753, NSF DMS-2010778

Acknowledgement

James Gee, Li Shen **University of Pennsylvania**

Jamie Hanson **University of Pittsburgh**

Shih-Gu Huang, Anqi Qiu **National University of Singapore**

Anass El Yaagoubi Bourakna, Hernando Ombao **KAUST,**
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Grants: NIH U01NS093650, NS117568, EB022856, EB028753, NSF DMS-2010778

Abstract

A new data-driven topological approach is presented for estimating state spaces in dynamically changing functional brain networks of humans. The approach penalizes the topological distance between networks and clusters, dynamically changing brain networks into topologically distinct states. The method considers the temporal dimension of the data through the Wasserstein distance between networks. The method is shown to outperform the widely used k-means clustering often used in estimating the state space in brain networks. The method is applied to accurately determine the state spaces of dynamically changing functional brain networks. Subsequently, the question of if the overall topology of brain networks is a heritable feature using the twin study design is addressed. The talk is based on [arXiv:2201.00087](https://arxiv.org/abs/2201.00087)(under review in *PLOS Computational Biology*)

Computational Neuroimaging

Neuroscience
+ Mathematics
+ Statistics
+ CS

Magnetic resonance imaging (MRI)



Wisconsin Twin Brain Imaging Study done here

3T GE Discovery X750
Waisman Brain Imaging Laboratory
University of Wisconsin-Madison

Magnetic Resonance Imaging (MRI)

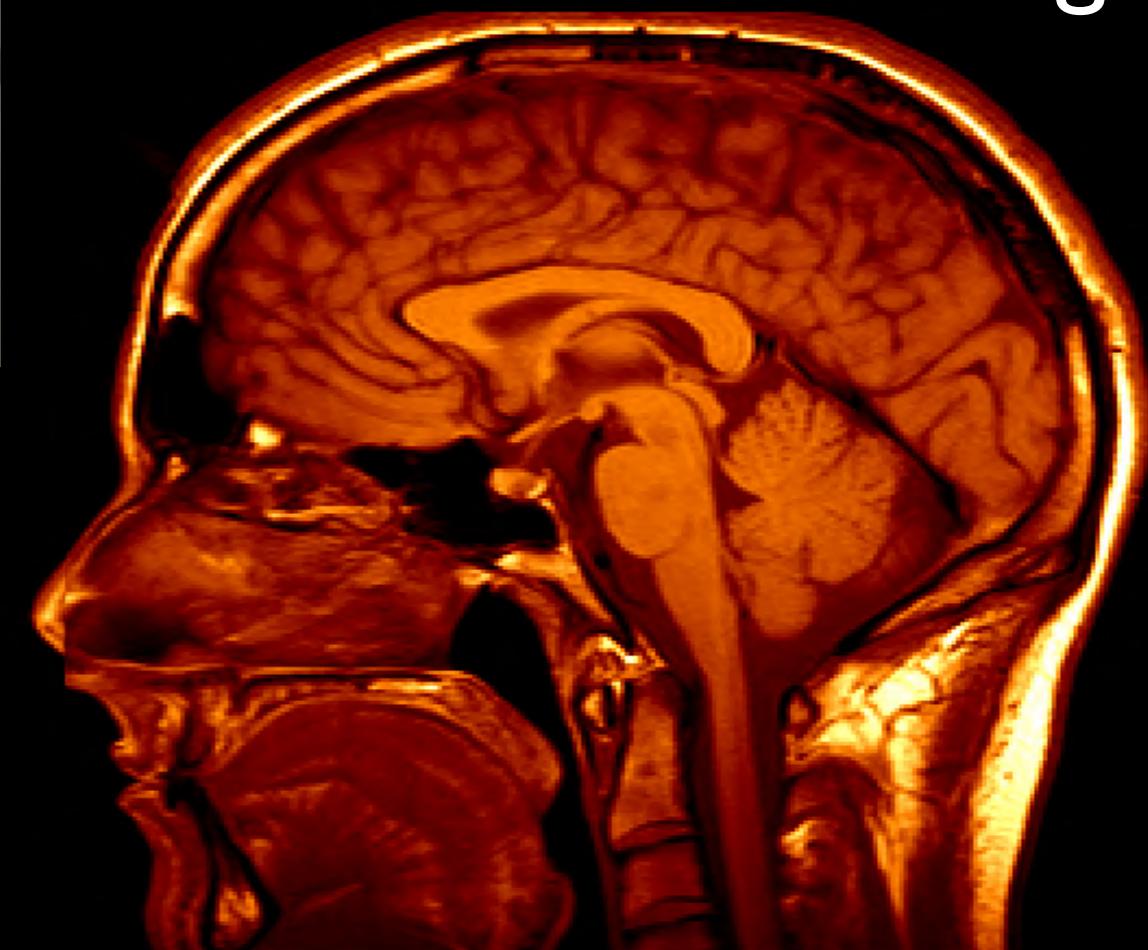


3.0 Tesla GE Scanner

Soft tissues: brain

Soft tissues

3D image

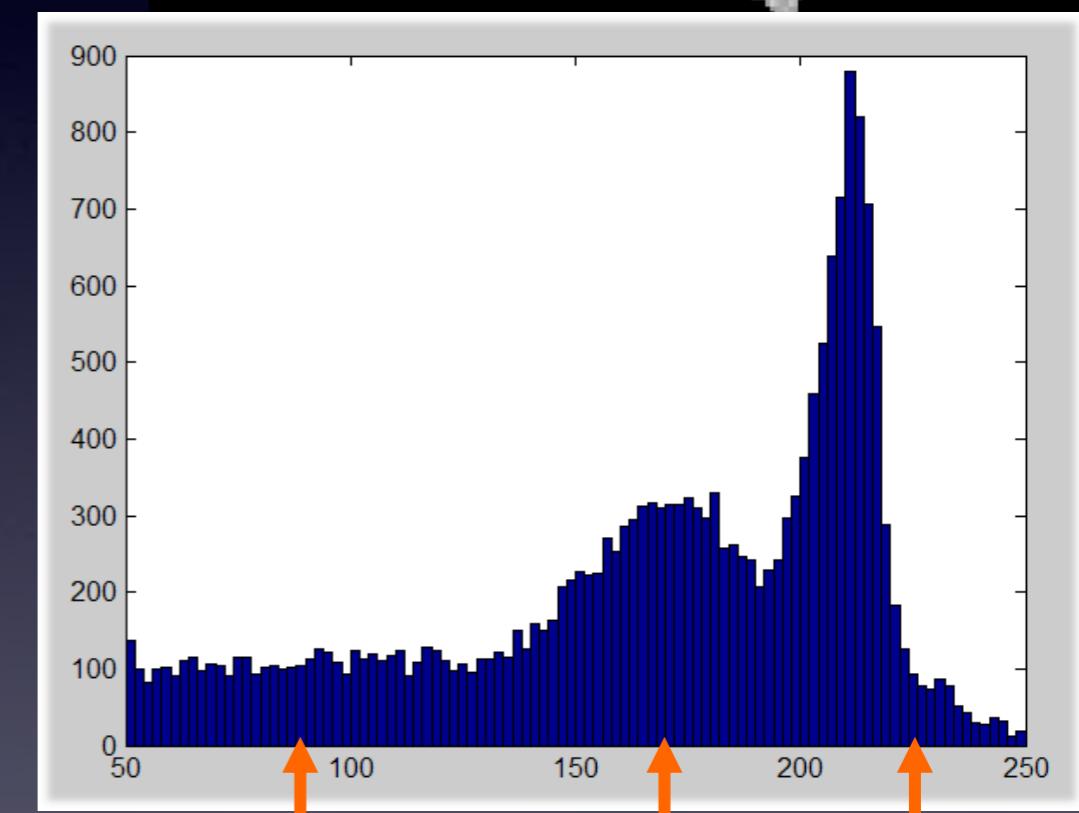
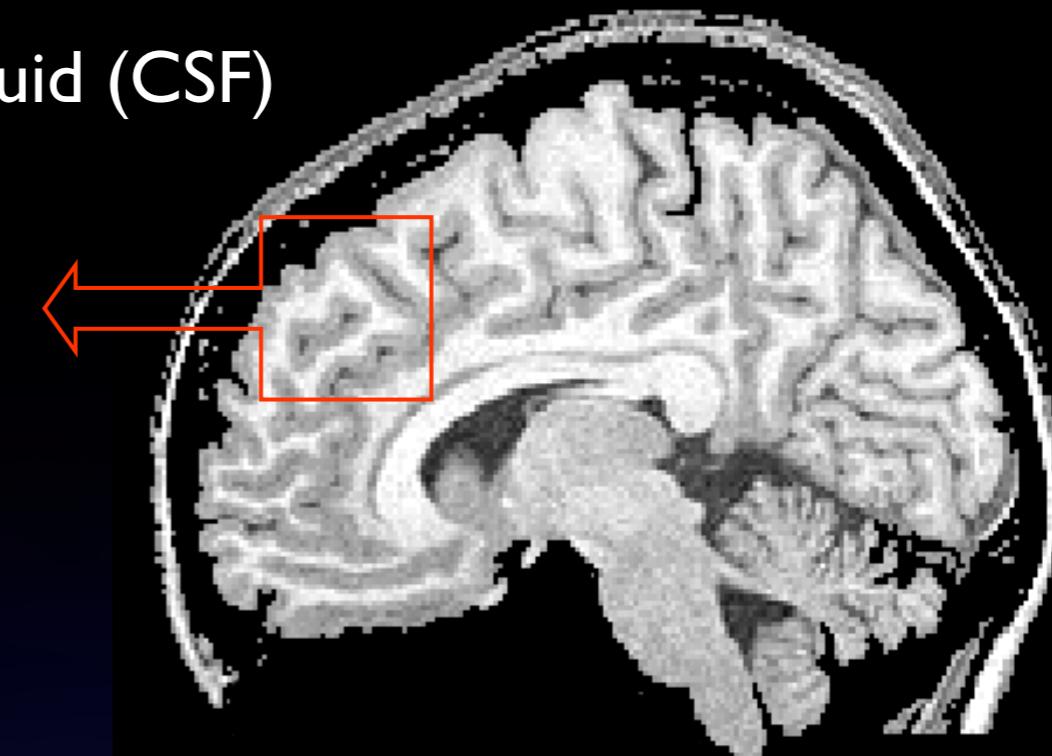
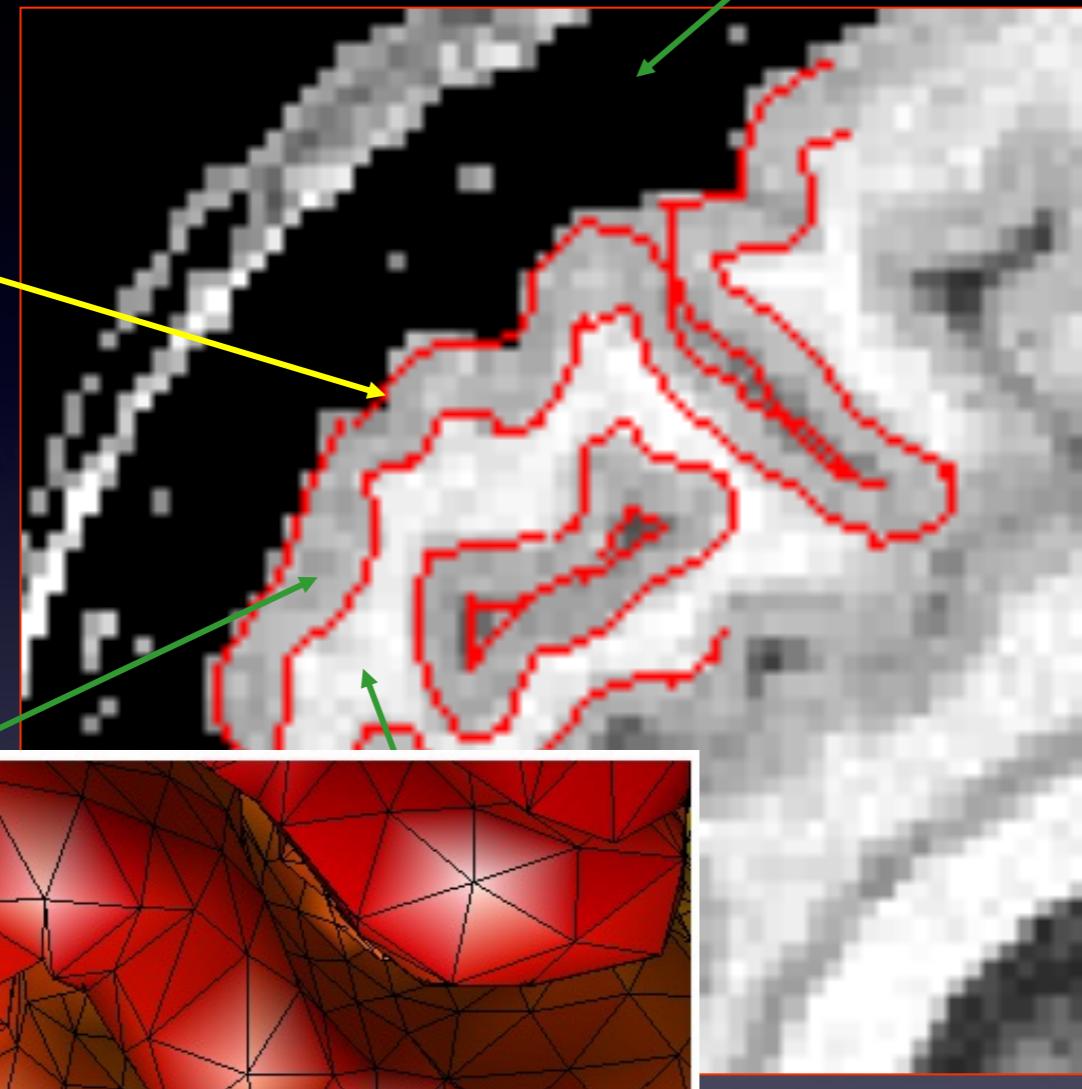


Basic brain anatomy

Cerebral Spinal Fluid (CSF)

Outer
Cortical
Surface

Gray

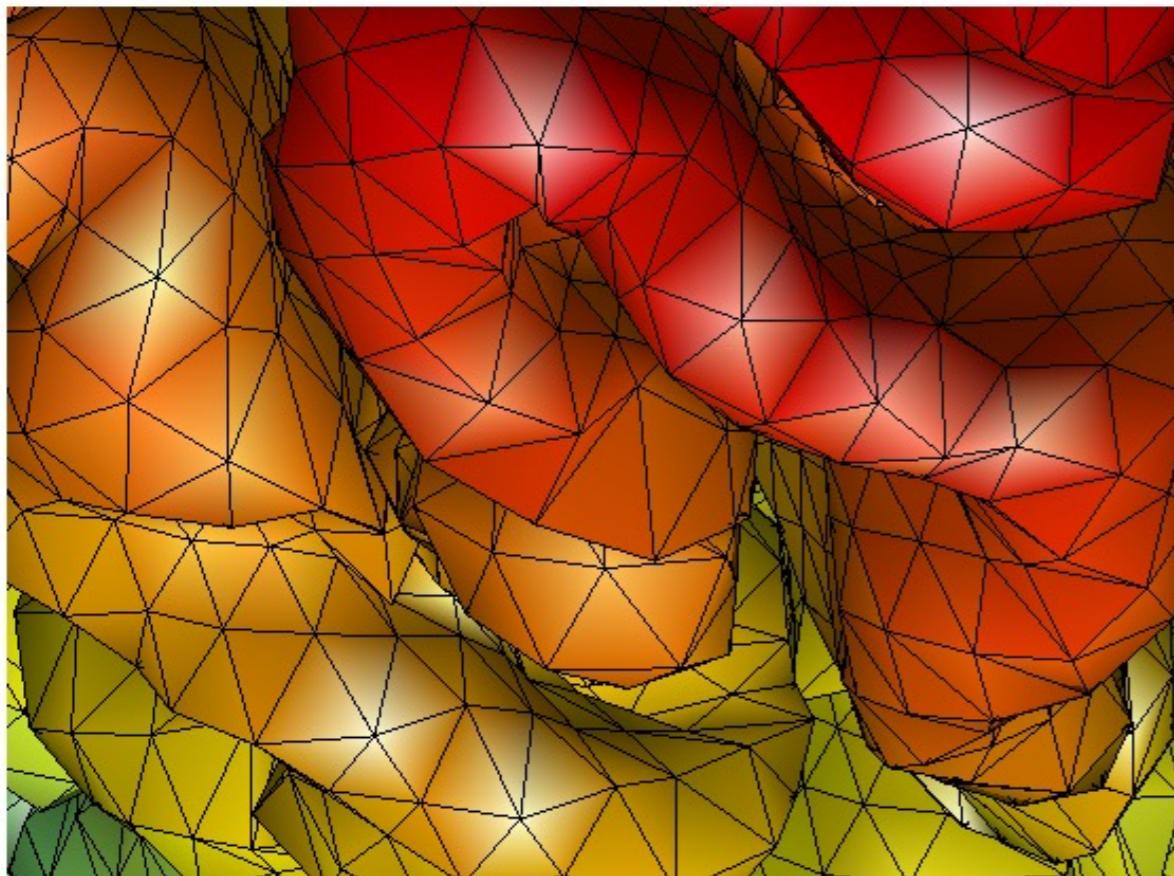


CSF

Gray

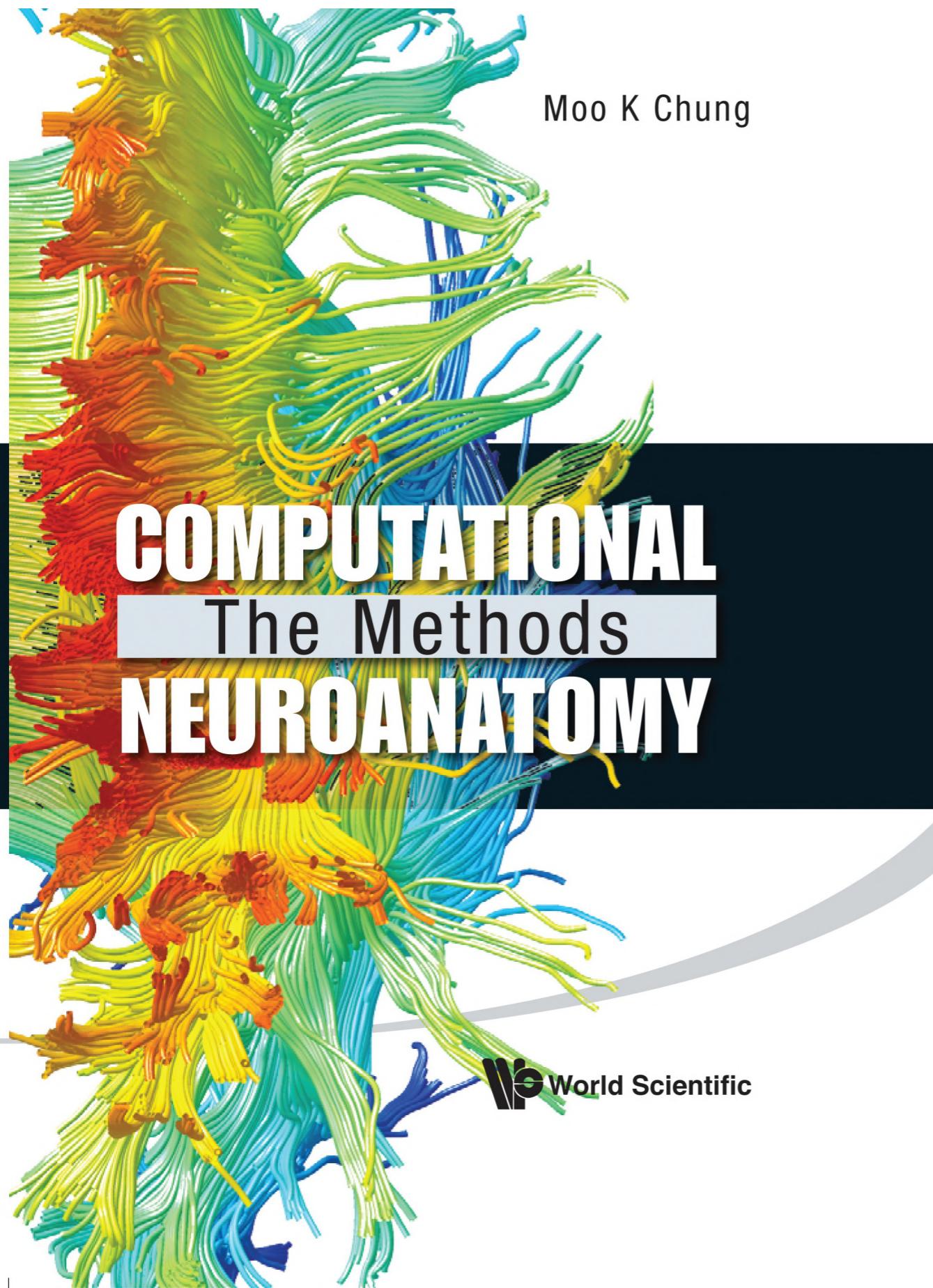
White

3 component Gaussian mixture



computational neuroanatomy

COMPUTATIONAL NEUROANATOMY



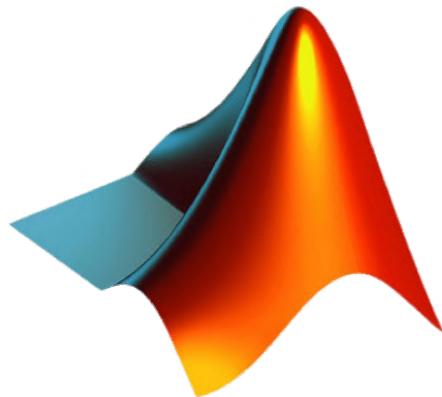
Mathematics
Computer Science
Statistics
Neuroimaging



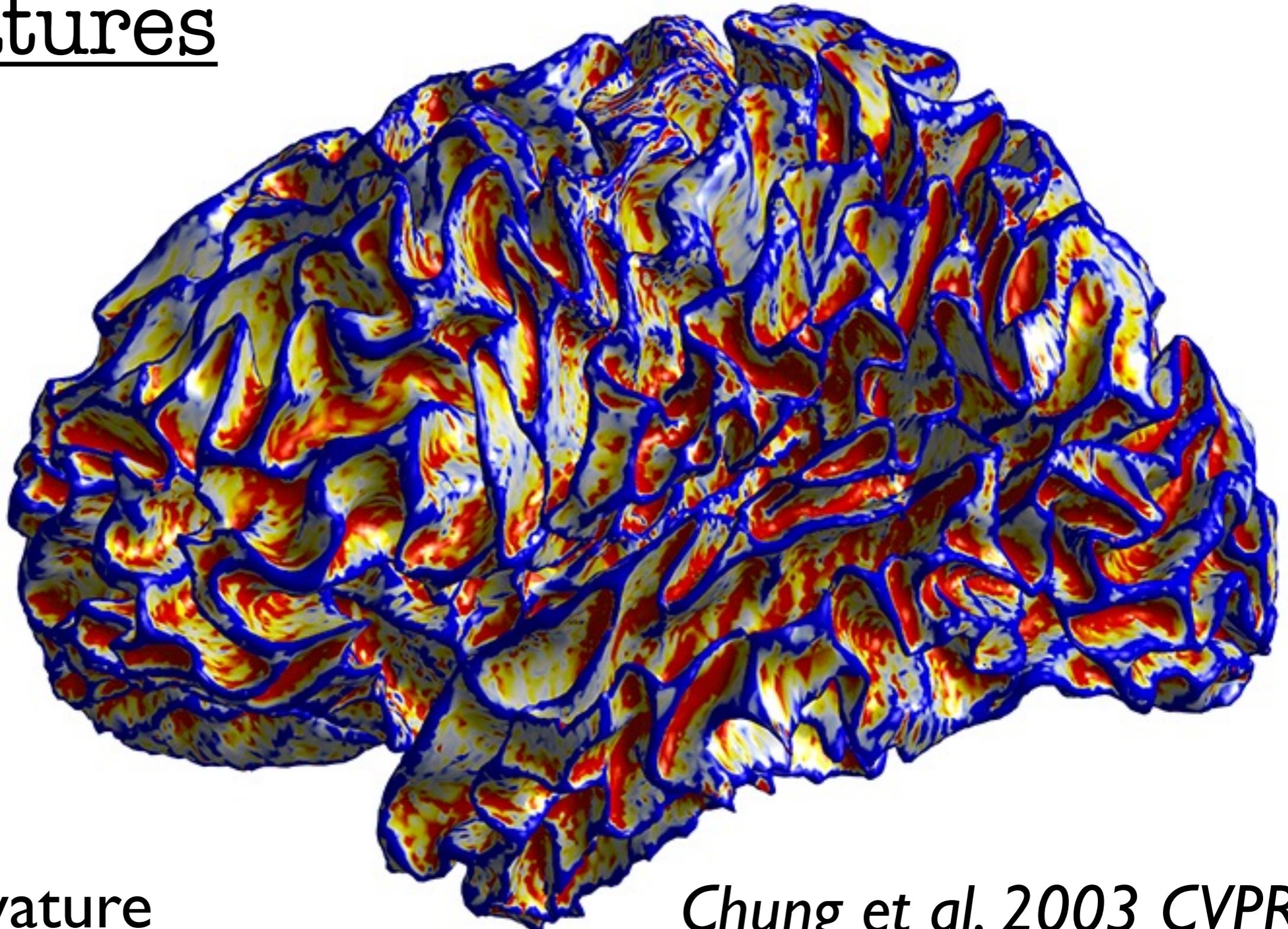
Quantification of
spatiotemporal dynamics
of anatomical shapes and
objects biomedical
images through
differential geometry

Code and sample data

[https://github.com/laplcebeltrami/
curvatures](https://github.com/laplcebeltrami/curvatures)



MATLAB®



Mean curvature

Chung et al. 2003 CVPR

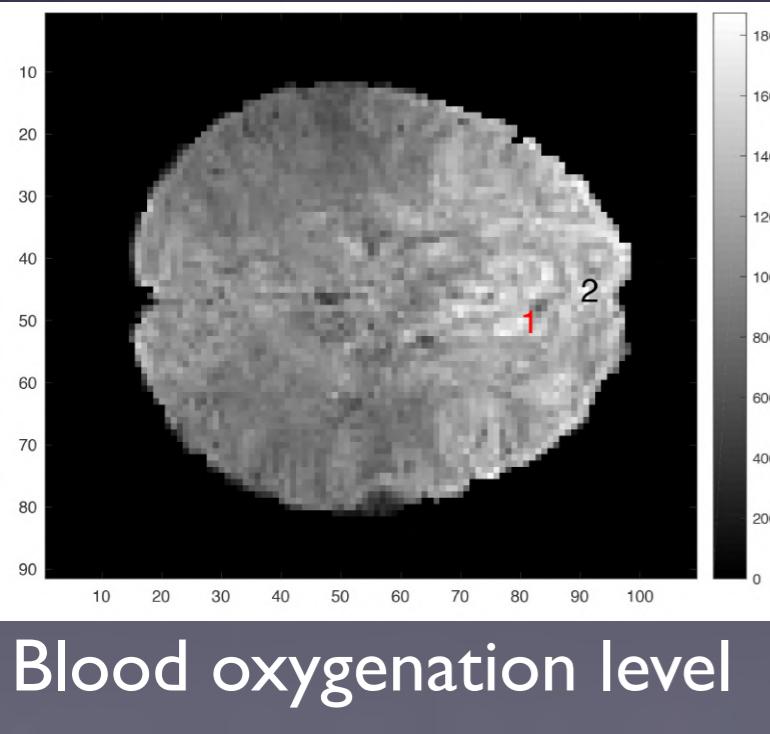
Functional Magnetic Resonance Imaging (fMRI)



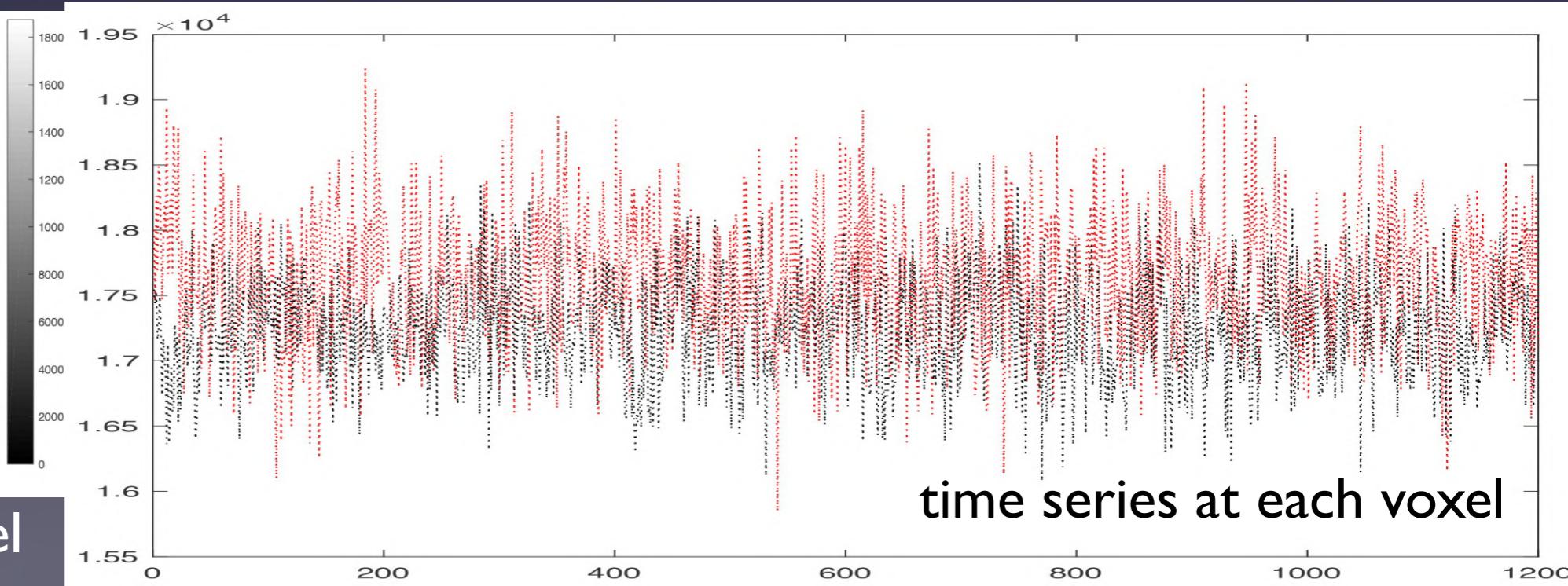
Resting-state fMRI at 300000 voxels per subject measured over 14min 33 seconds inside a scanner

416 subjects (131 MZ twins
77 DZ twins) \times 2GB = **832GB data**

3.0 Tesla GE Scanner

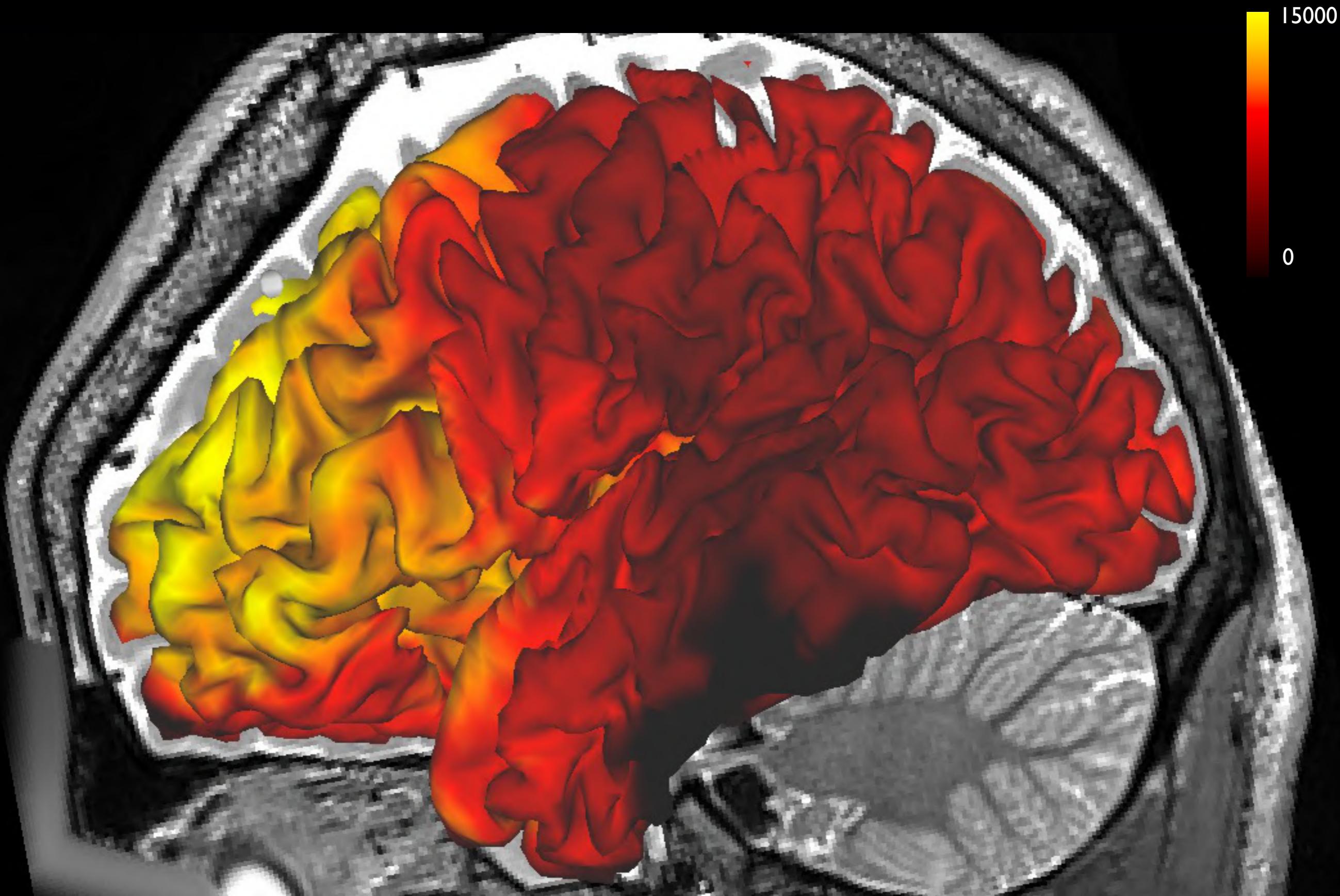


Blood oxygenation level



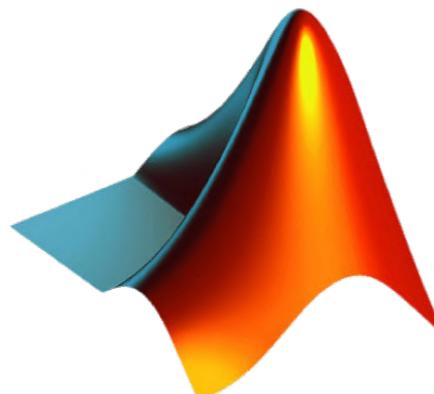
time series at each voxel

Typical rs-fMRI (every 30 second)

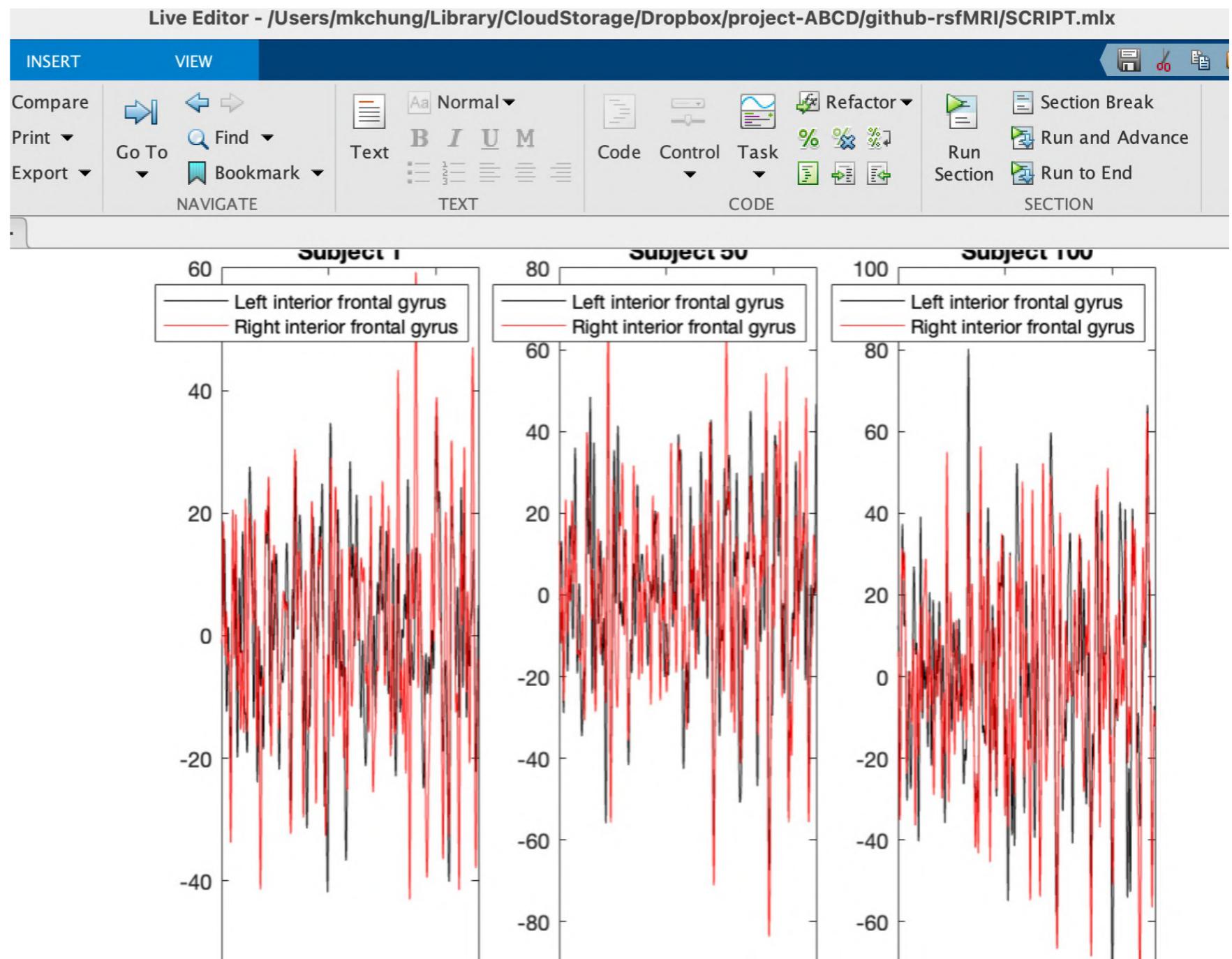


Code and sample data

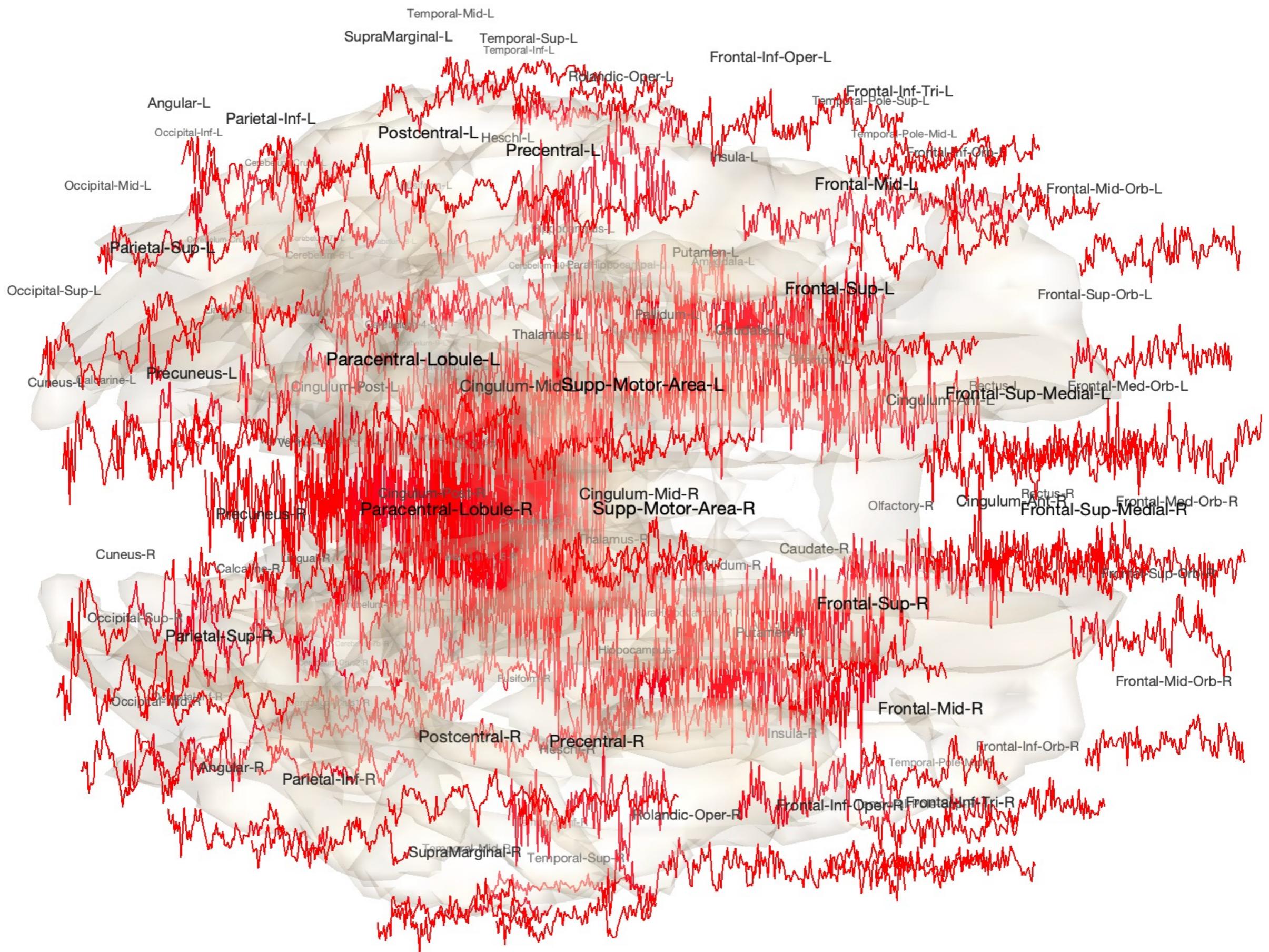
[https://github.com/laplcebeltrami/
rsfMRI](https://github.com/laplcebeltrami/rsfMRI)



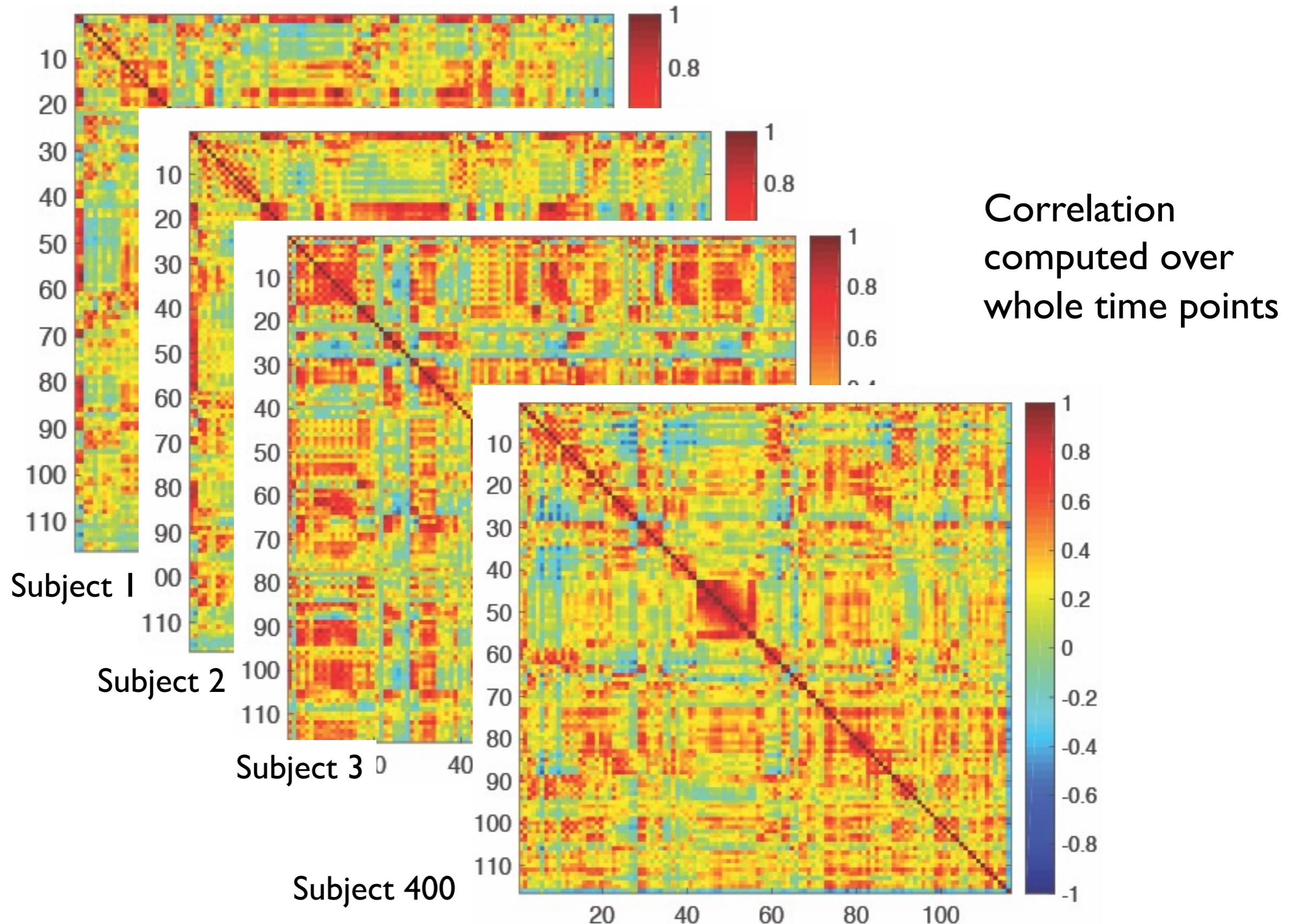
MATLAB®



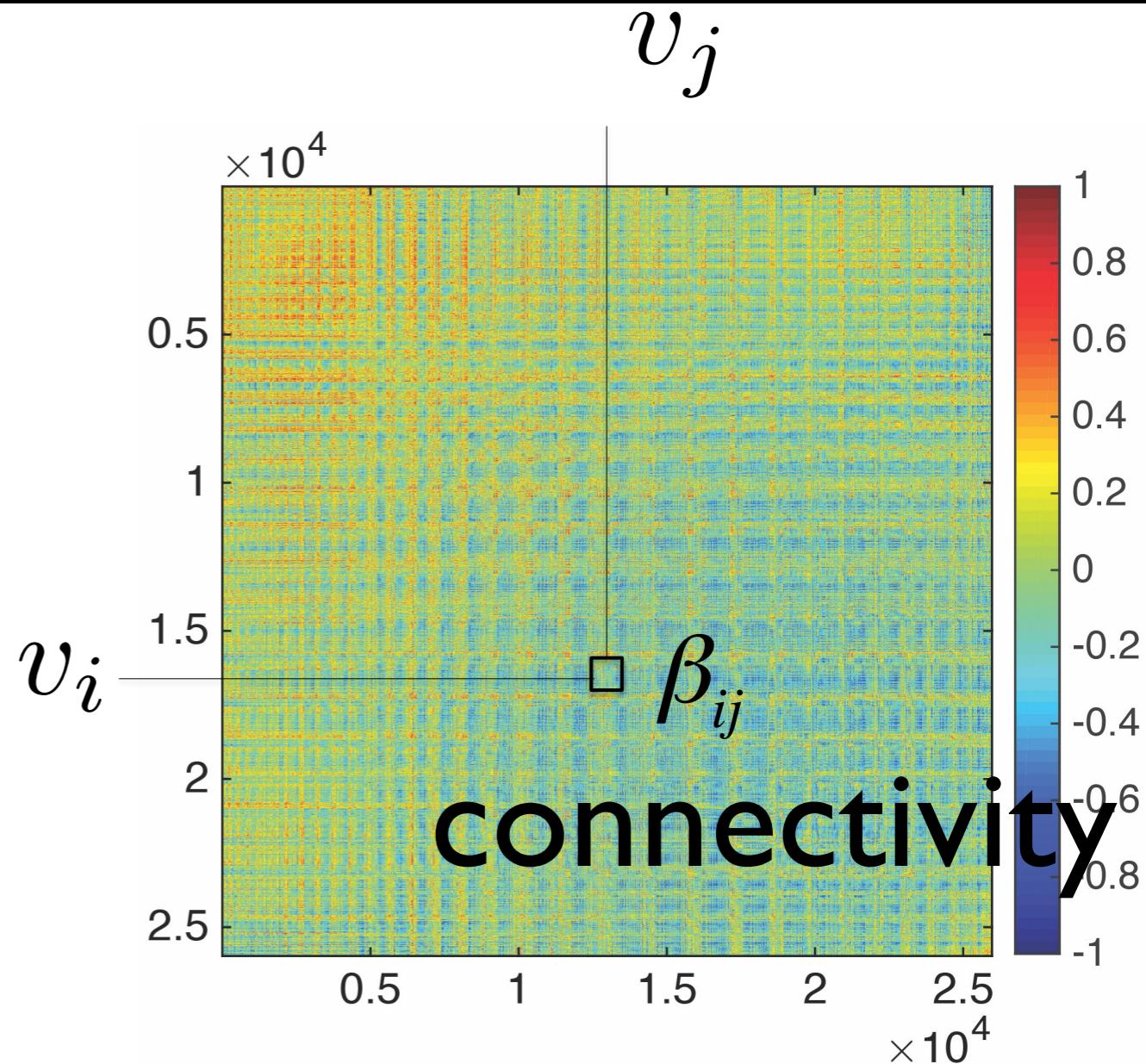
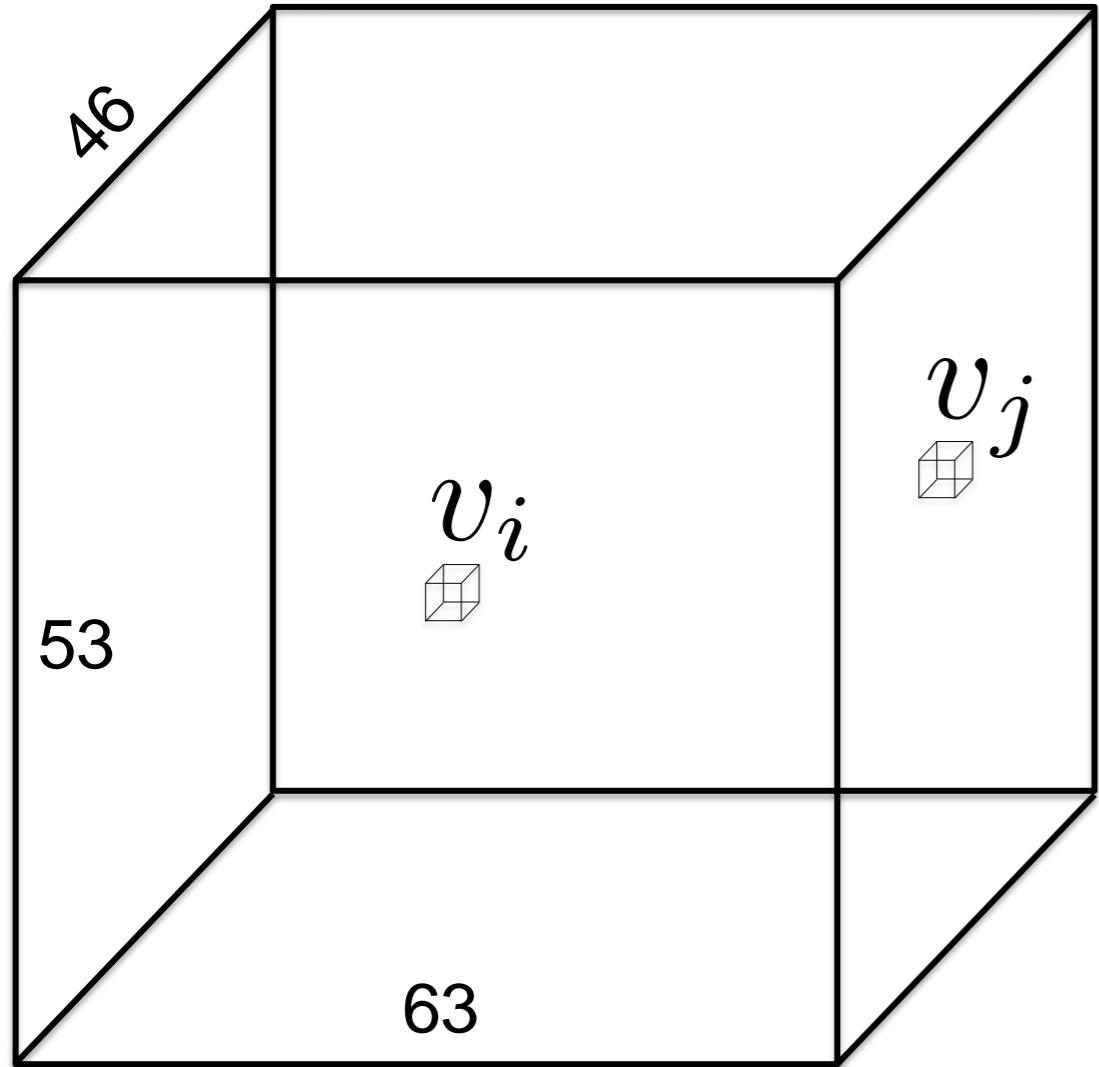
Time series averaged into 116 brain regions



Subject level brain connectivity matrix

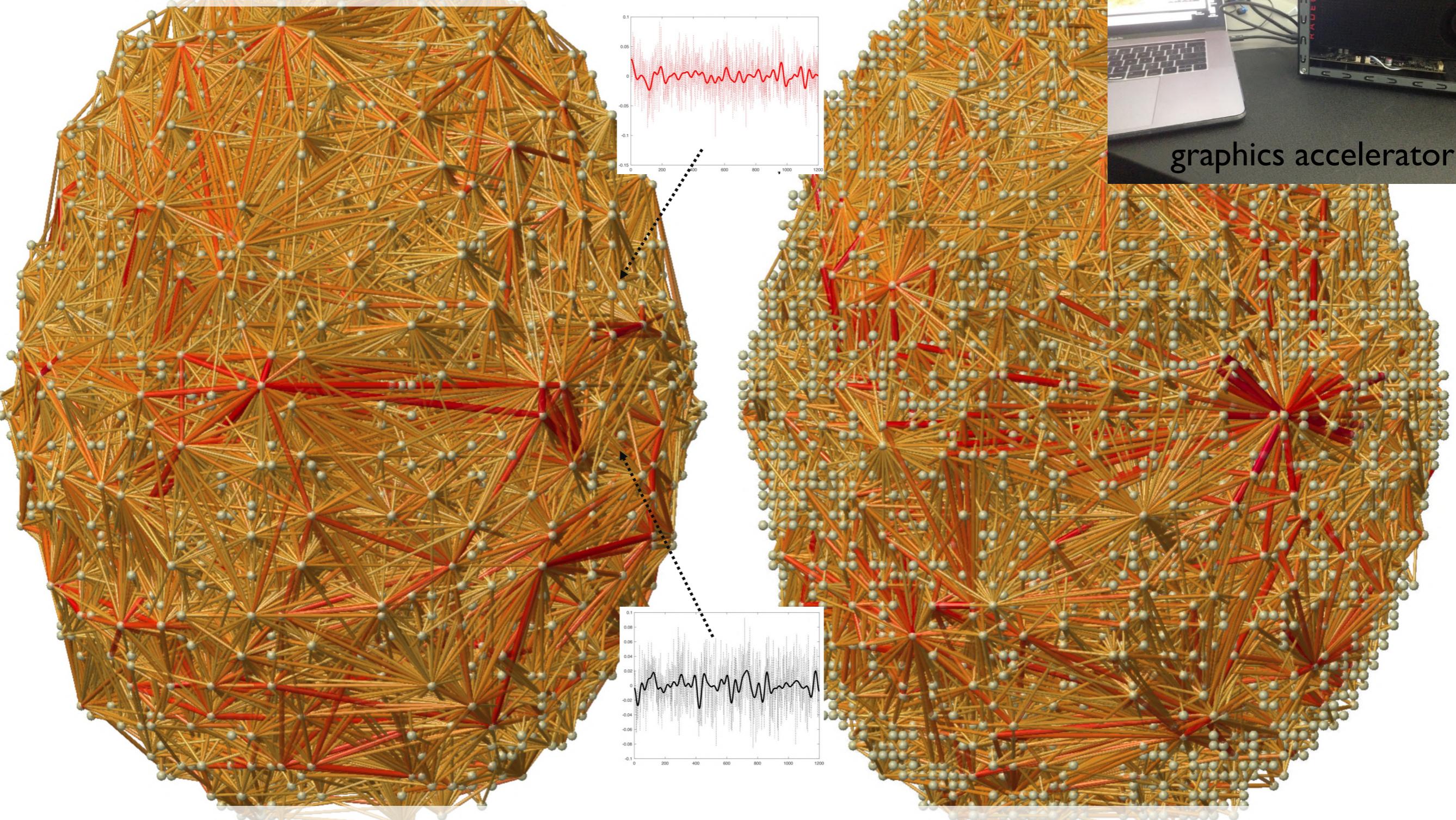


How big is fMRI connectivity data?



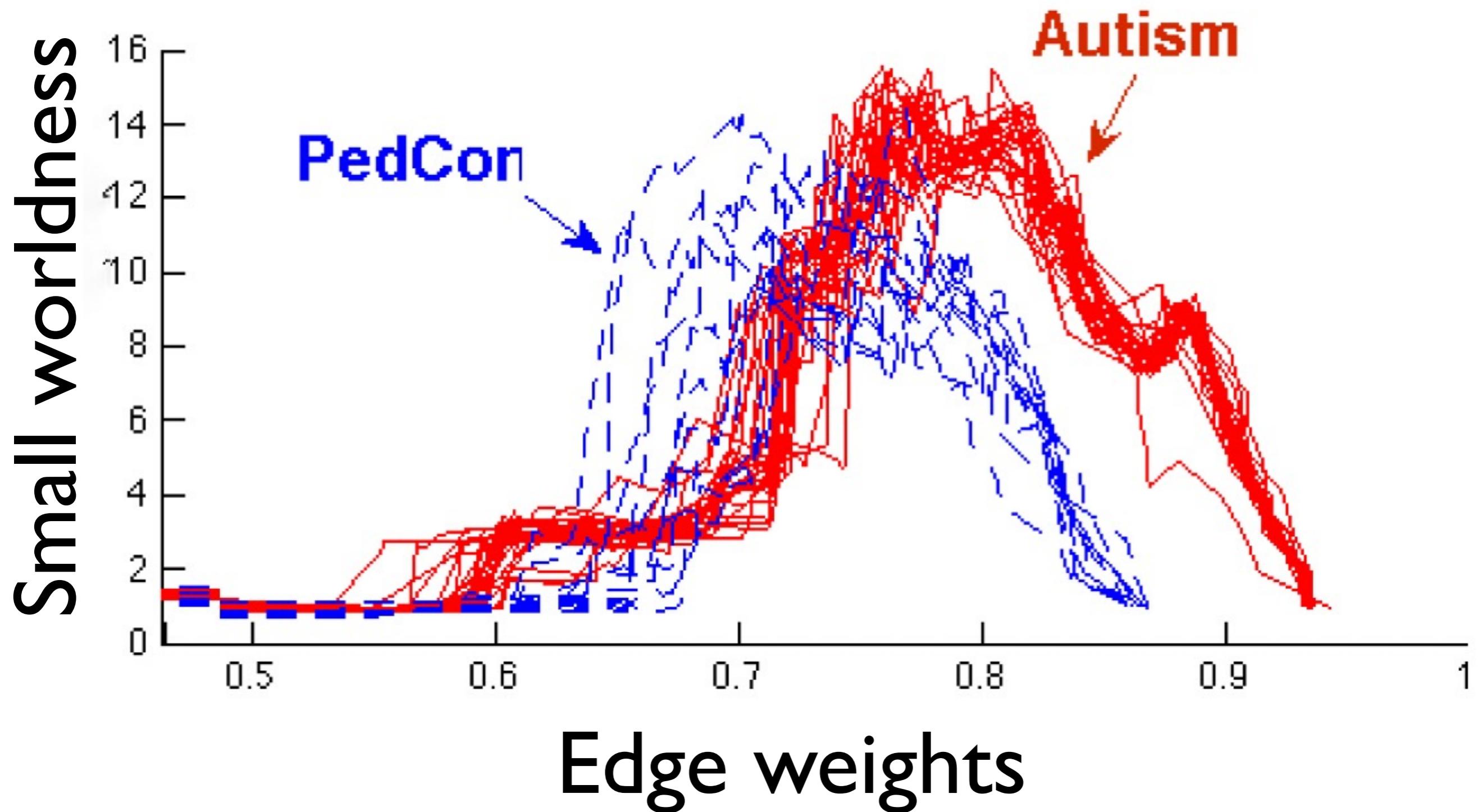
$p=25972$ voxels (1.5T at 3mm resolution) in the brain
 $25972 \times 25972 = 0.67$ billion connections
5.2GB data

Big data computation

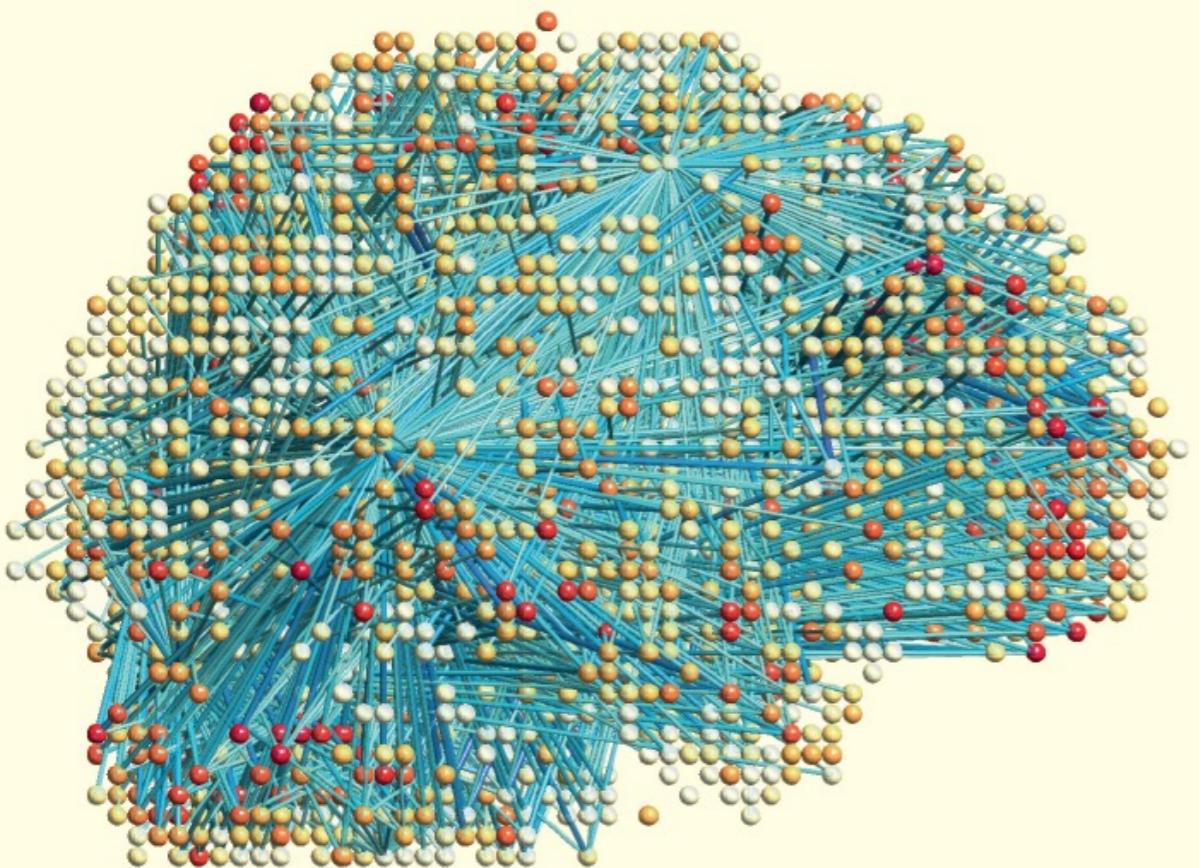


Resting state brain network obtained from functional-MRI.
Correlation of **300000** time series in the brain.
For 3D rendering, subsampled at **25000** nodes.

Graph theory features → Often incorrect conclusion



BRAIN NETWORK ANALYSIS



Moo K. CHUNG

Book writing with
Cambridge University
Press on tutorial style
applied-TDA

Chung, 2019
Cambridge University Press

Topological data analysis (TDA)

Completely data driven!
No model!
No distributional assumption!

Chung et al., 2009
Information Processing
in Medical Imaging
(IPMI) 5636:386-397.

Surface Data

L. Kim⁴

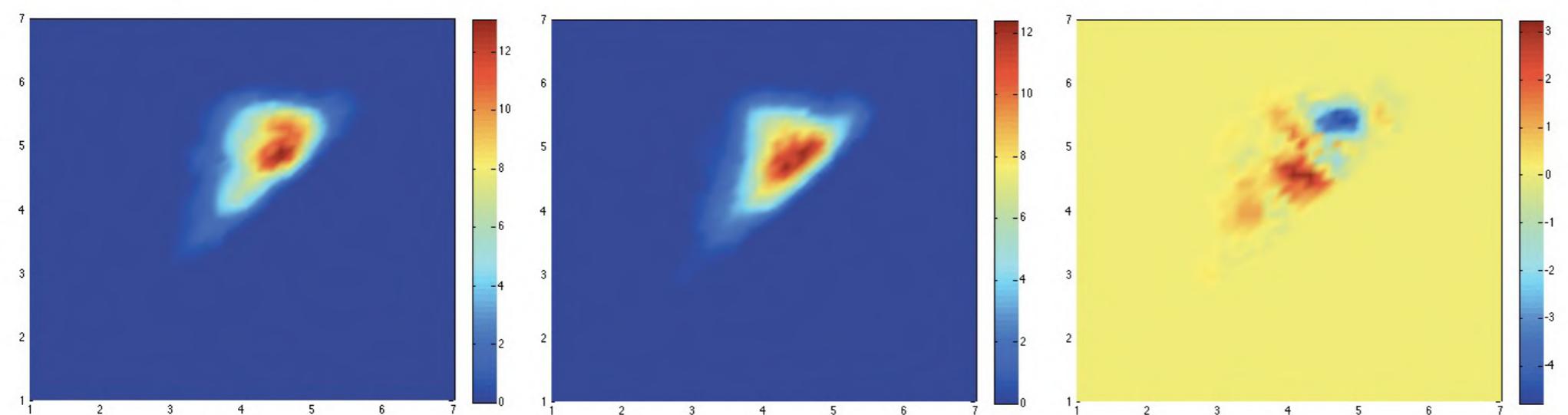
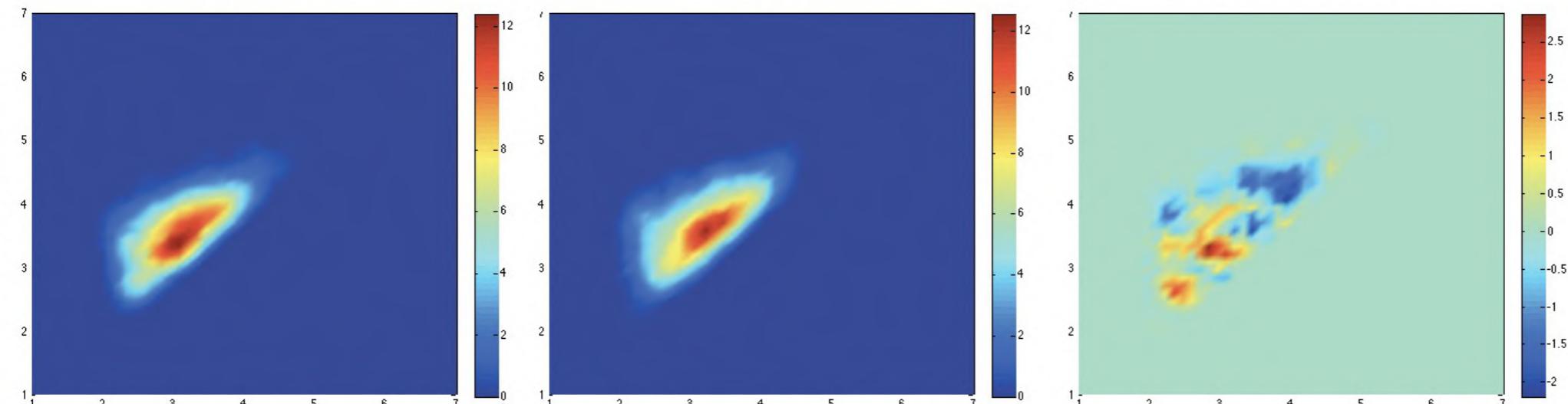
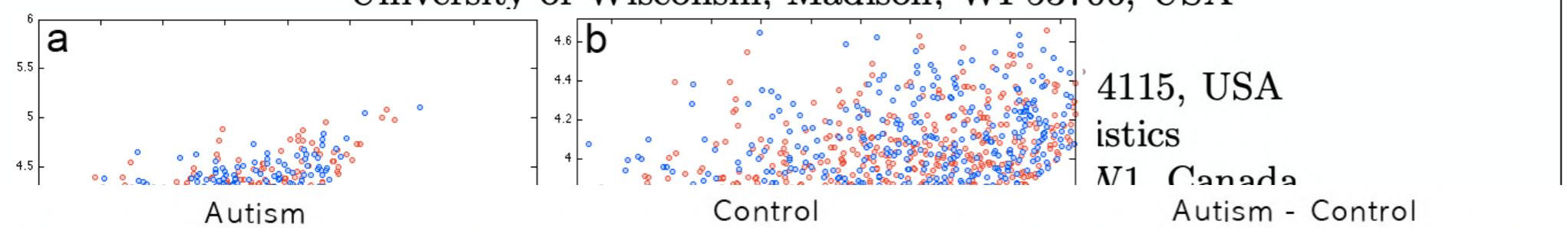
natics
behavior
JSA

4115, USA

istics

M1 Canada

Autism - Control



First TDA paper
in medical
imaging

After 14 years
and 50 TDA
papers later ...

Matlab toolbox PH-STAT

Statistical Inference on Persistent Homology
Code written with Chat-GPT

<https://github.com/laplcebeltrami/PH-STAT>

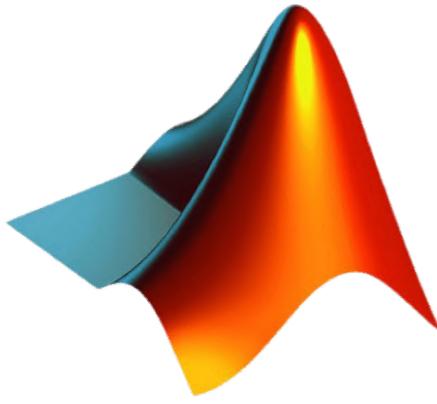
Manual:

Chung (and CHAT-GPT) 2023, PH-STAT [arXiv:2304.05912](https://arxiv.org/abs/2304.05912)

The codes are used to publish topological data analysis papers in leading journals and conferences since 2009:

IEEE Transactions on Medical Imaging, NeuroImage, Human Brain Mapping, Network Neuroscience, Annals of Applied Statistics, Information Processing in Medical Imaging (IPMI), MICCAI, ISBI

<https://github.com/laplcebeltrami/PH-STAT>



MATLAB®

Planning for
NIH tool
development grant

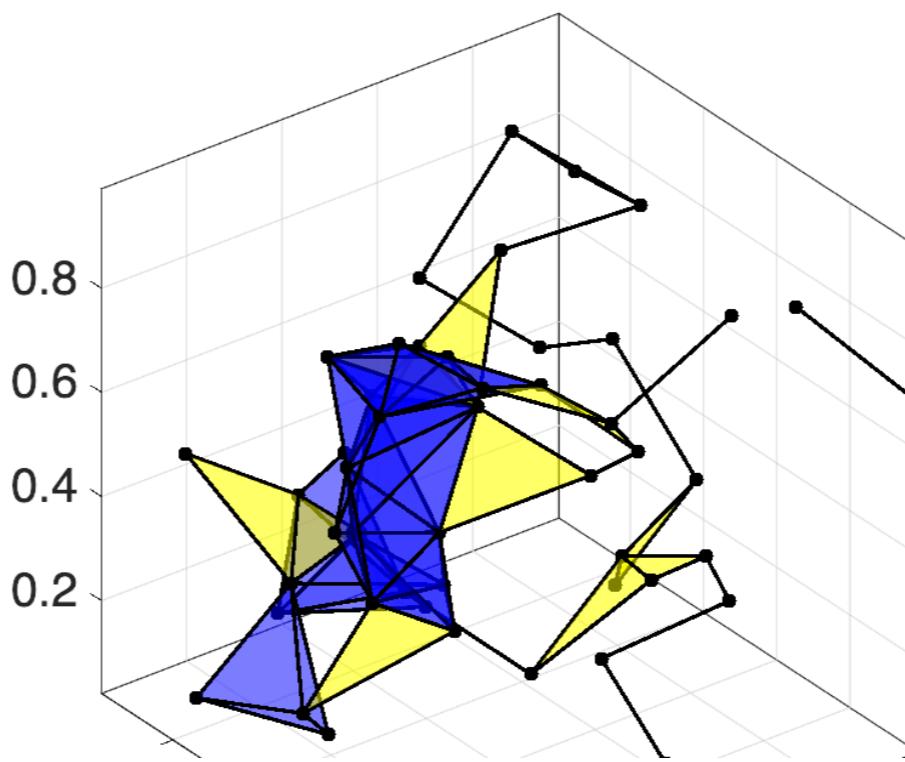
Live Editor - /Users/mkchung/Library/CloudStorage/Dropbox/PH-STAT/SCRIPT.mlx

The screenshot shows the MATLAB Live Editor interface with a blue header bar. The menu bar includes 'R', 'INSERT', 'FIGURE', 'VIEW', 'FILE', 'NAVIGATE', 'TEXT', 'CODE', 'SECTION', and 'Run'. The main area contains the following MATLAB code:

```
%Display Rips complex
PH_rips_display(X,S);
%labels = cellstr(num2str((1:p)', '% d'));
%text(X(:,1)+0.01, X(:,2)+0.01, X(:,3)+0.01, labels, 'Color', 'r', 'FontSize',16)

% Boundary matrices
B = PH_boundary(S);
betti = PH_boundary_betti(B);
title(['Betti numbers=' num2str(betti)])|
```

Betti numbers=3 4 0



<https://github.com/laplcebeltrami/PH-STAT>

New simplicial complex data structure for brain networks

Structured/cell array can handle variable length data.

```
rng(2023); %fixed random seeds  
p=50; d=3; %p=# of nodes, d=dimension  
X = rand(p, d); %random in a cube  
radius = 0.3;  
S= PH_rips(X,d,radius) %Rips complex
```

How to build *functions on top of simplicial complexes*

```
S =  
4x2 cell array  
 { 50x1 double} { 50x1 double}  
 {101x2 double} {101x1 double}  
 { 73x3 double} { 73x1 double}  
 { 27x4 double} { 27x1 double}
```

```
[S{1,1} S{1,2}] =
```

1	0
2	0
3	0
4	0
5	0

%node
indexing

%function
on nodes

How to build *hierarchical lexicological indexing*

[S{2,1} S{2,2}] =

1.0000	5.0000	0.2176
1.0000	9.0000	0.2823
1.0000	13.0000	0.1338
...		
5.0000	13.0000	0.2932

%Edge indexing

%function on edges

[S{3,1} S{3,2}] =

1.0000	5.0000	13.0000	0.2932
1.0000	5.0000	16.0000	0.2579
1.0000	5.0000	26.0000	0.2766
1.0000	5.0000	41.0000	0.2963

%face indexing

%function on faces

Graph Filtrations

most often used baseline in brain imaging

Weighted complete graph

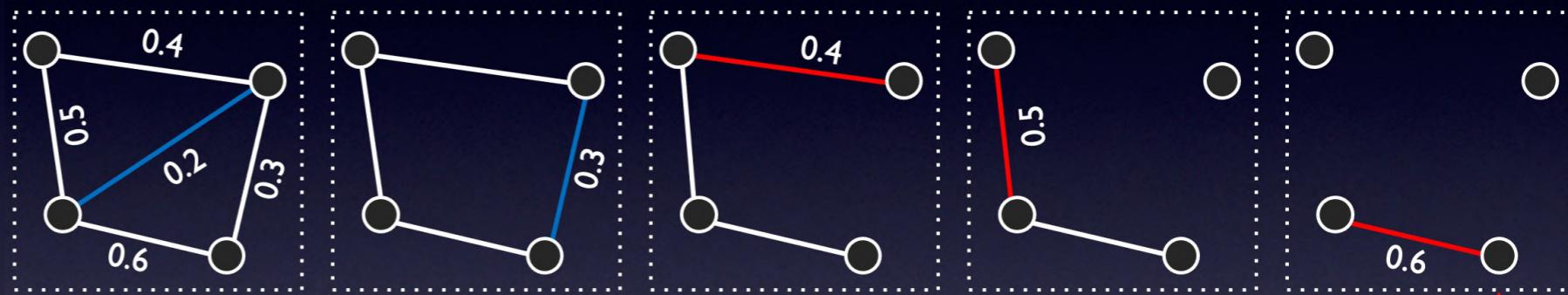
$$\mathcal{X} = (V, w) \quad w = (w_{ij})$$

Node set Edge weight

Binary graph

$$\mathcal{X}_\epsilon = (V, w_\epsilon)$$

$$w_{\epsilon,ij} = \begin{cases} 1 & \text{if } w_{ij} > \epsilon; \\ 0 & \text{otherwise.} \end{cases}$$



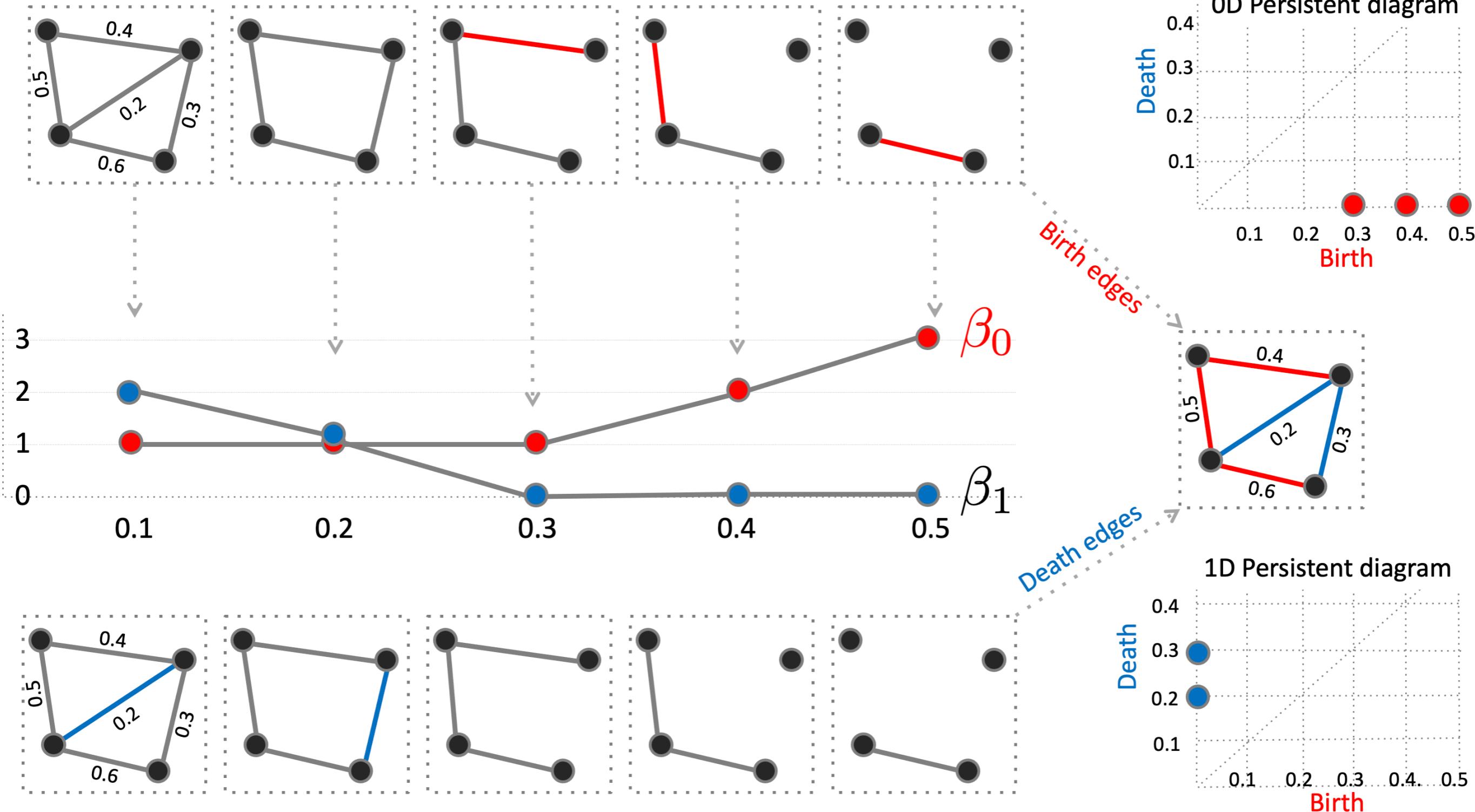
Graph filtration

$$\mathcal{X}_{\epsilon_0} \supset \mathcal{X}_{\epsilon_1} \supset \mathcal{X}_{\epsilon_2} \supset \cdots$$

for increased edge weights
 $\epsilon_0 < \epsilon_1 < \epsilon_2 < \cdots$

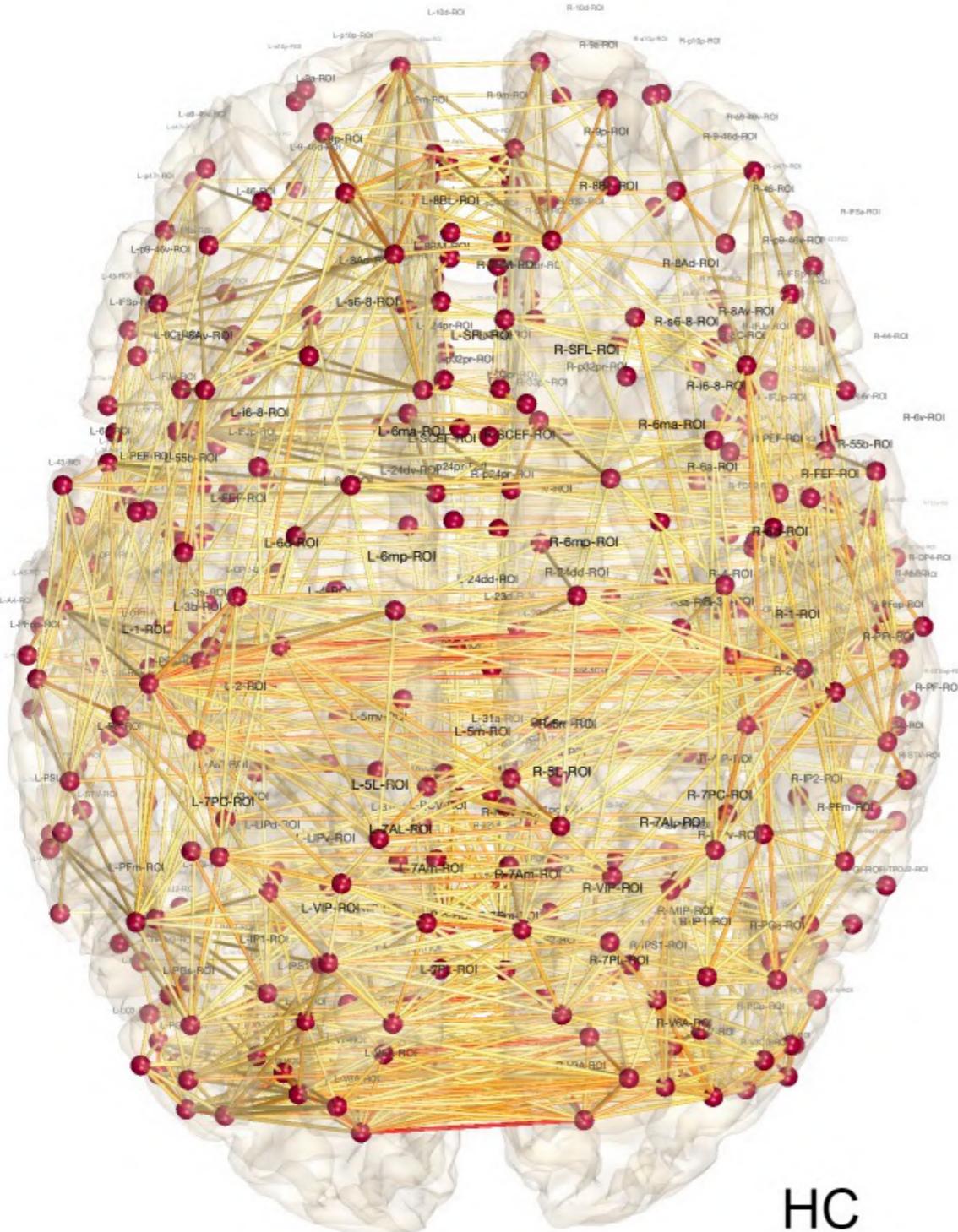
Equivalent to Rips filtration on radius $1 - \epsilon$ on 1-skeleton

Theorem: Birth & death decomposition

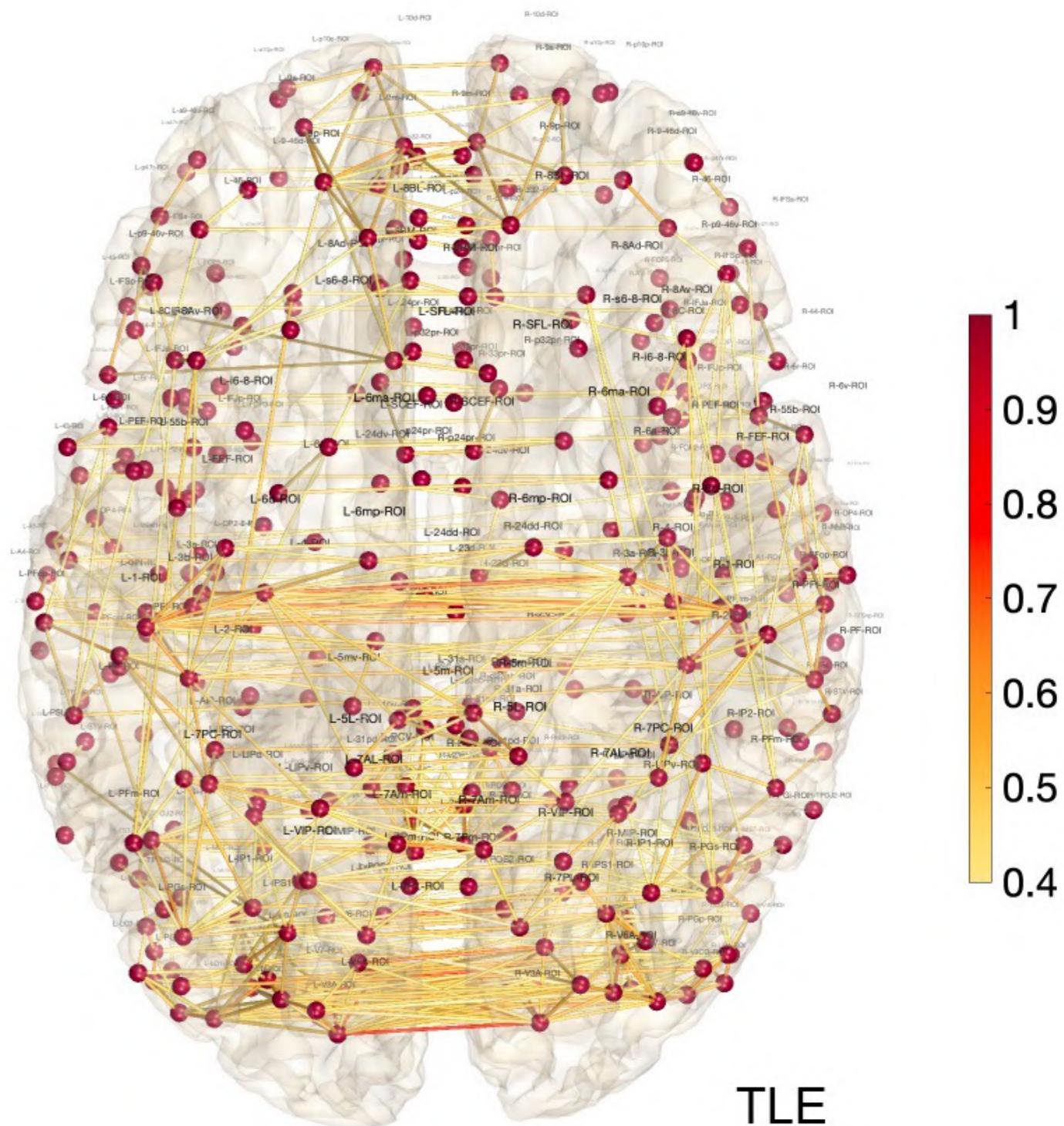


Average correlation networks

50 healthy controls



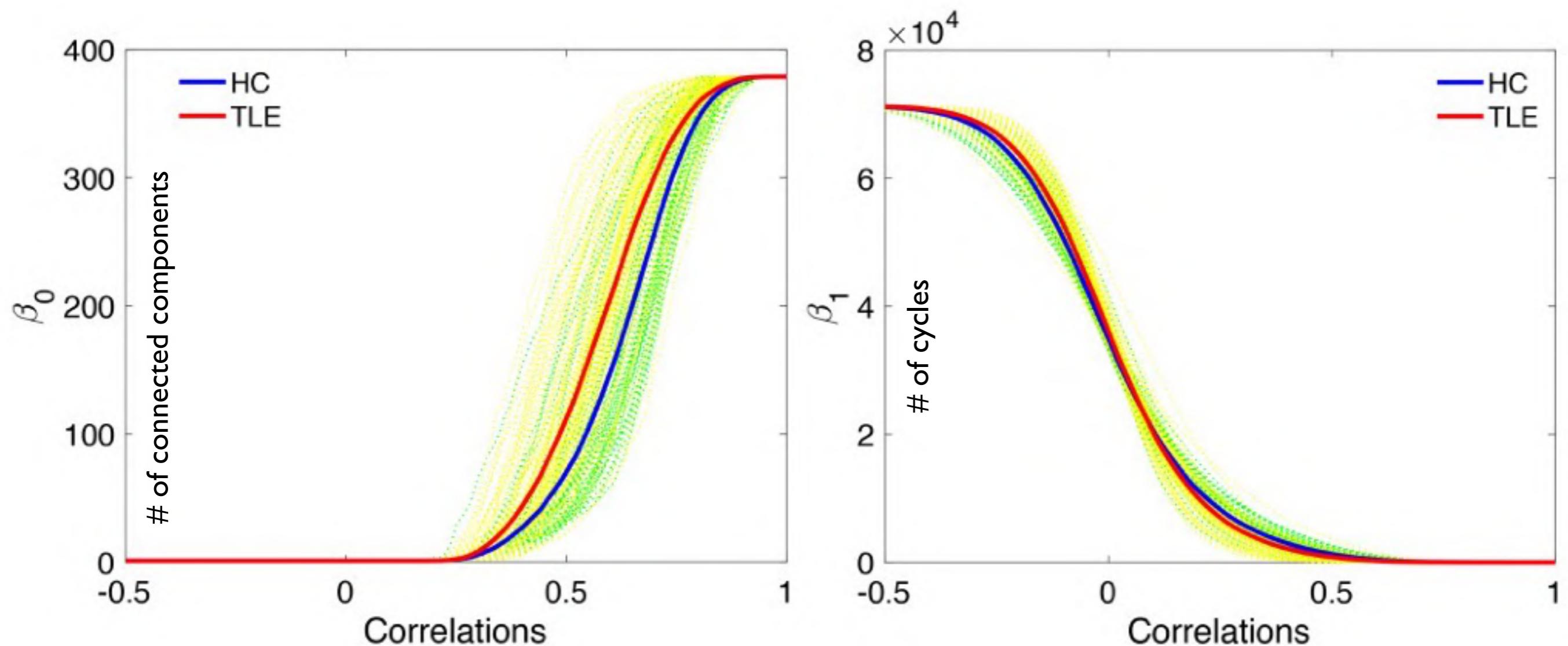
101 temporal lobe epilepsy



How much they differ topologically?

Betti curves

healthy controls (HC) vs. temporal lobe epilepsy (TLE)



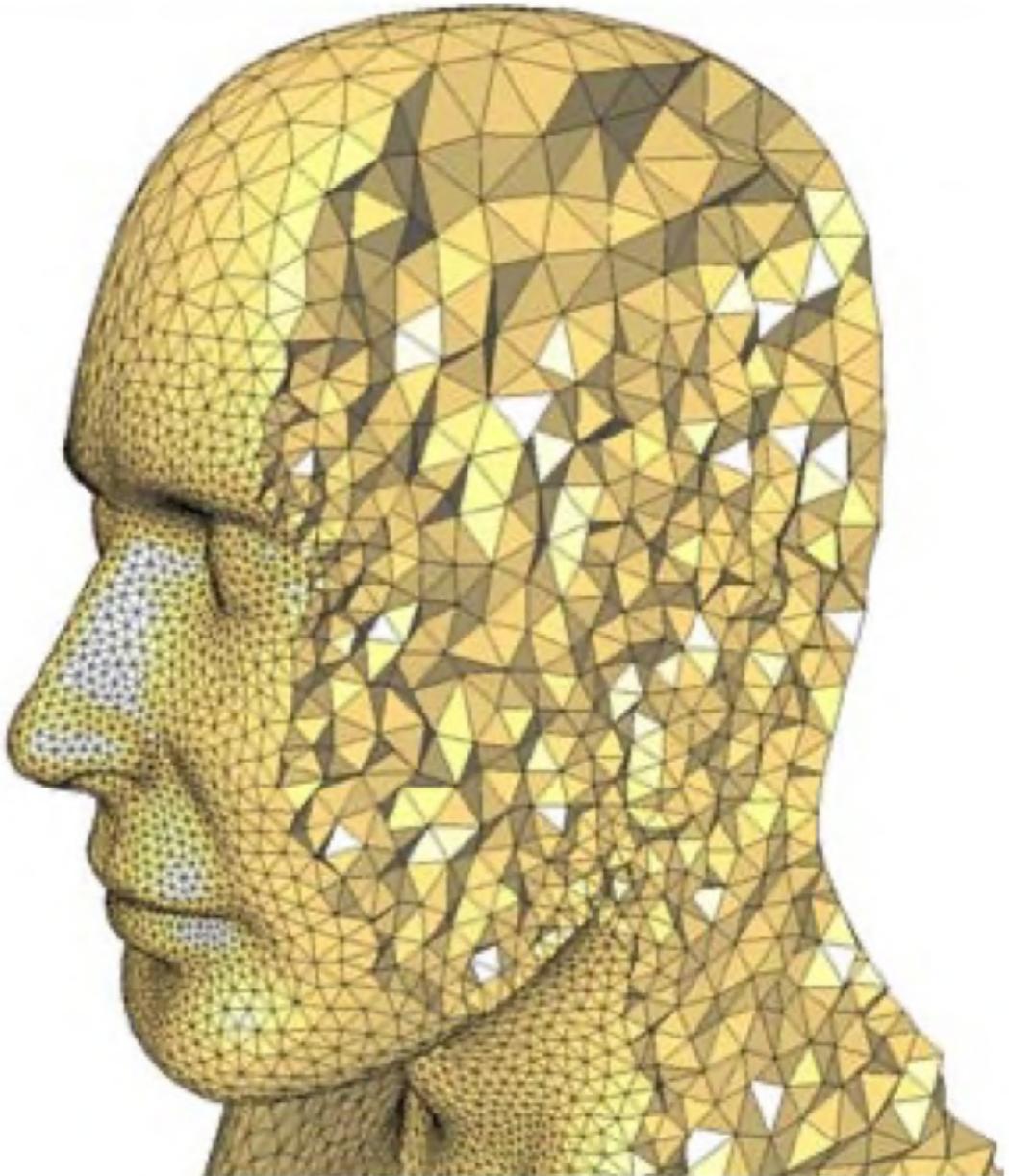
TLE has more disjoint subnetworks.

Open research problem

Can we extend the graph filtration to higher dimensional simplices such that

β_2, β_3, \dots are monotone?

Example: Tetrahedral mesh



2-Wasserstein distance between scatter points

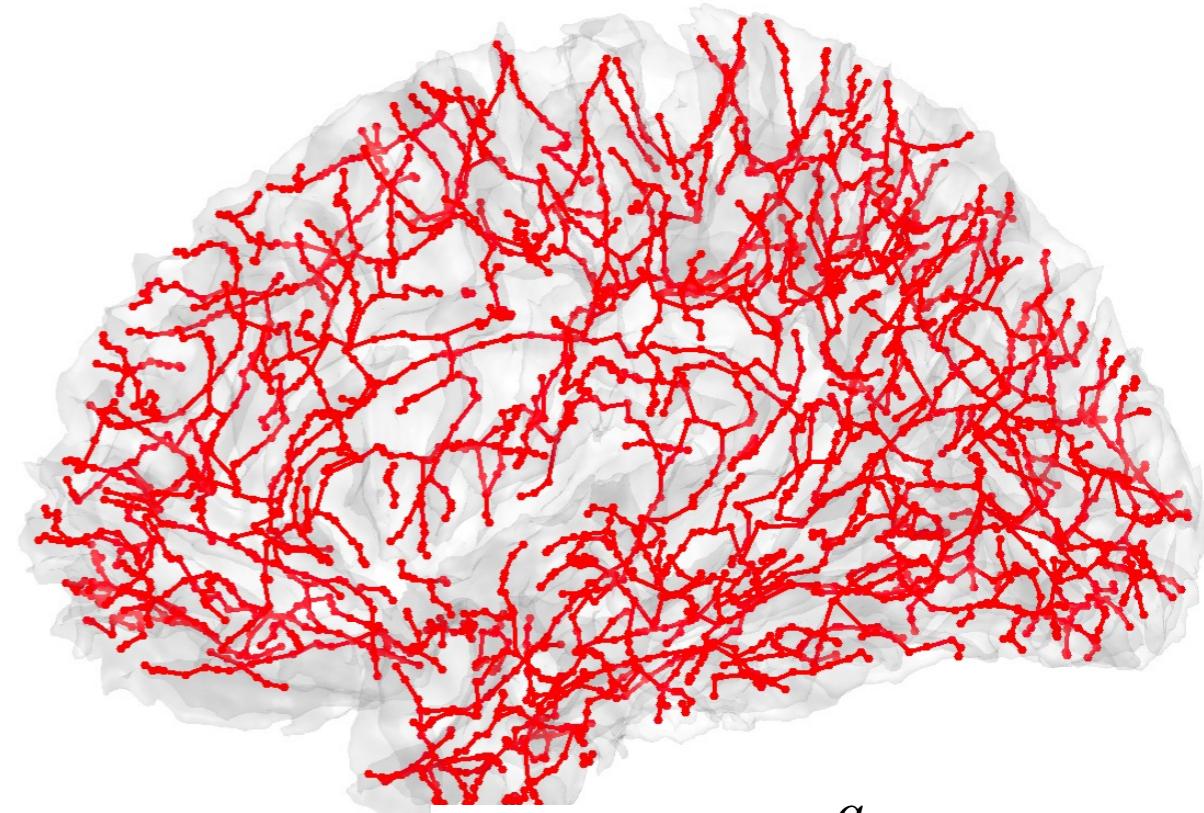
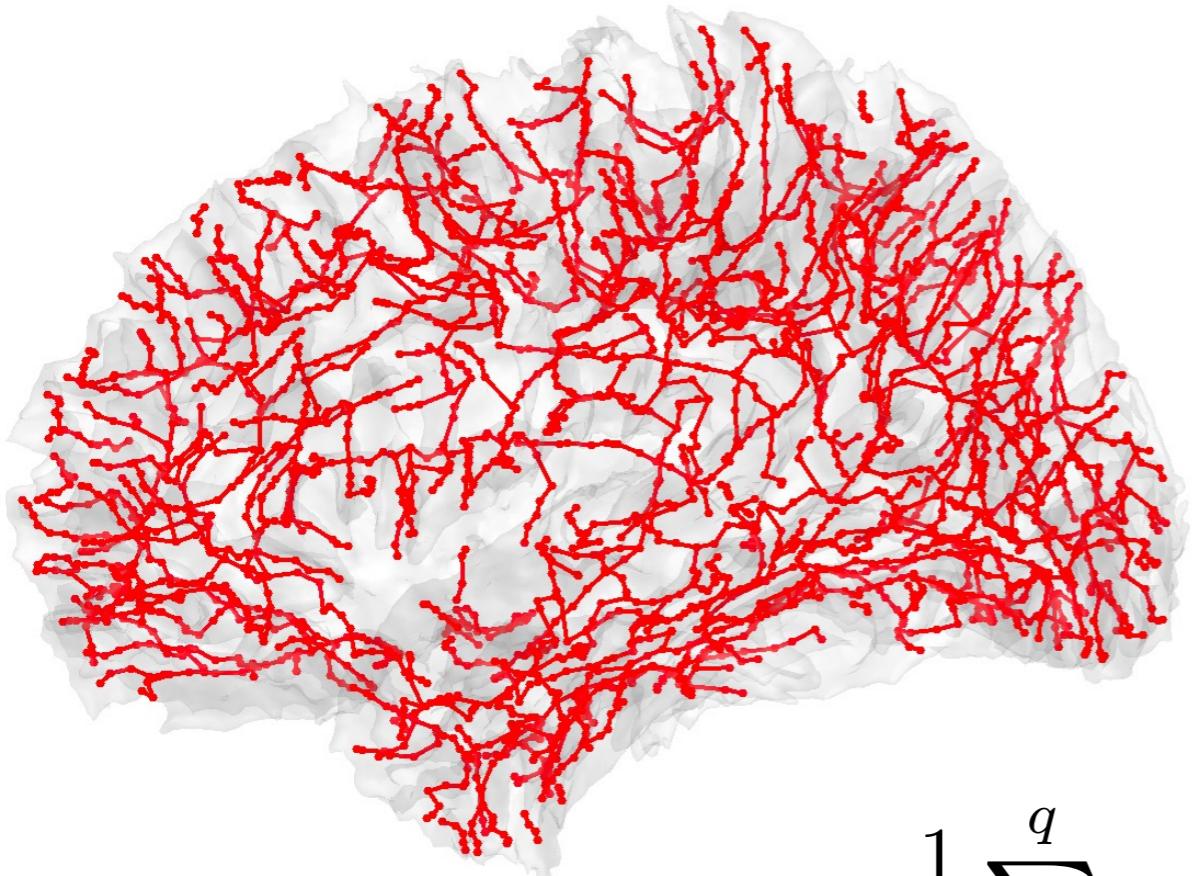
Random variables:

$$X \sim f_1$$

$$Y \sim f_2$$

2-Wasserstein distance:

$$\mathcal{D}(X, Y) = \left(\inf \mathbb{E} \|X - Y\|^2 \right)^{1/2}$$



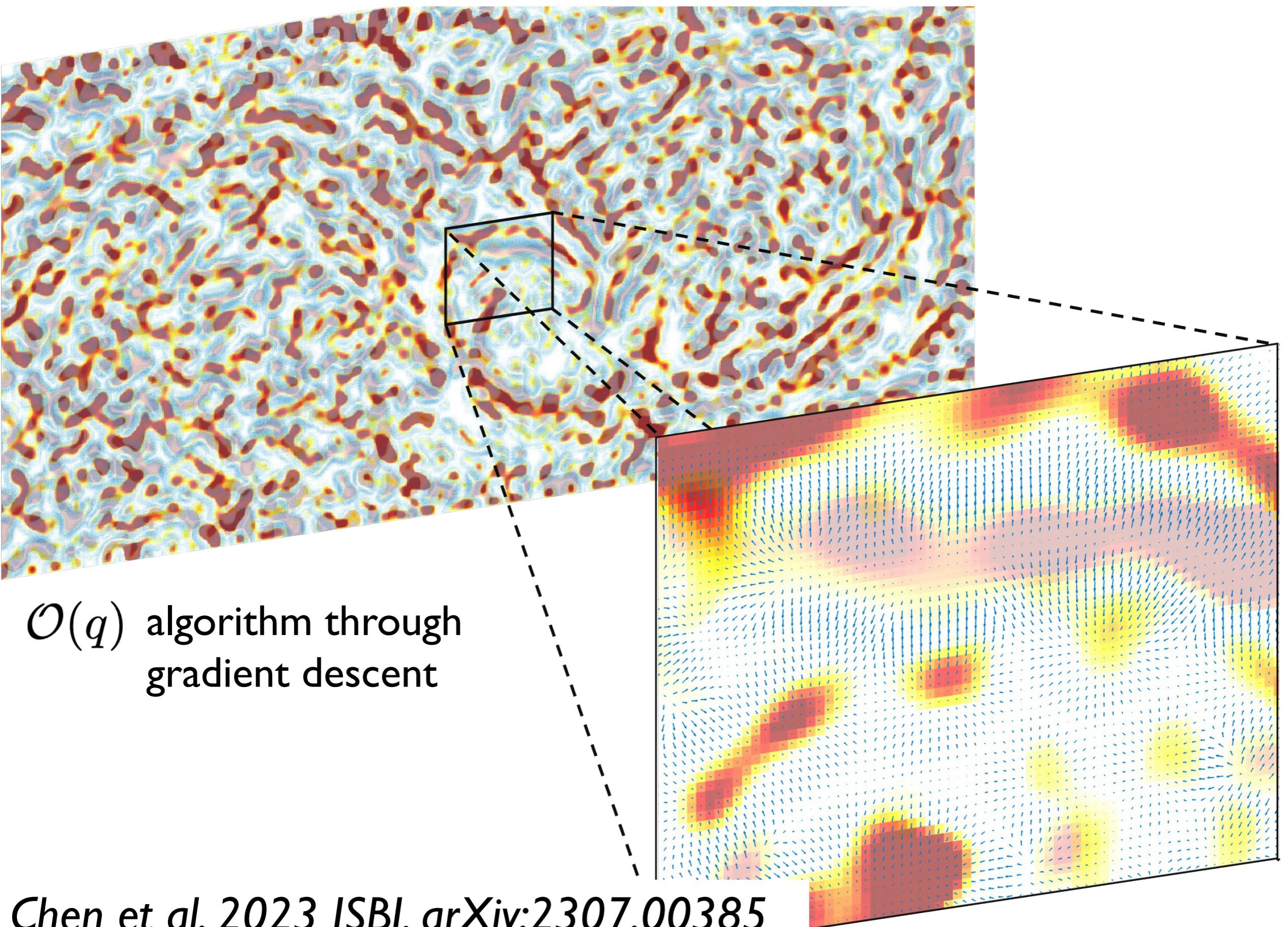
$$f_1(x) = \frac{1}{q} \sum_{i=1}^q \delta(x - x_i)$$

$$f_2(y) = \frac{1}{q} \sum_{i=1}^q \delta(y - y_i)$$

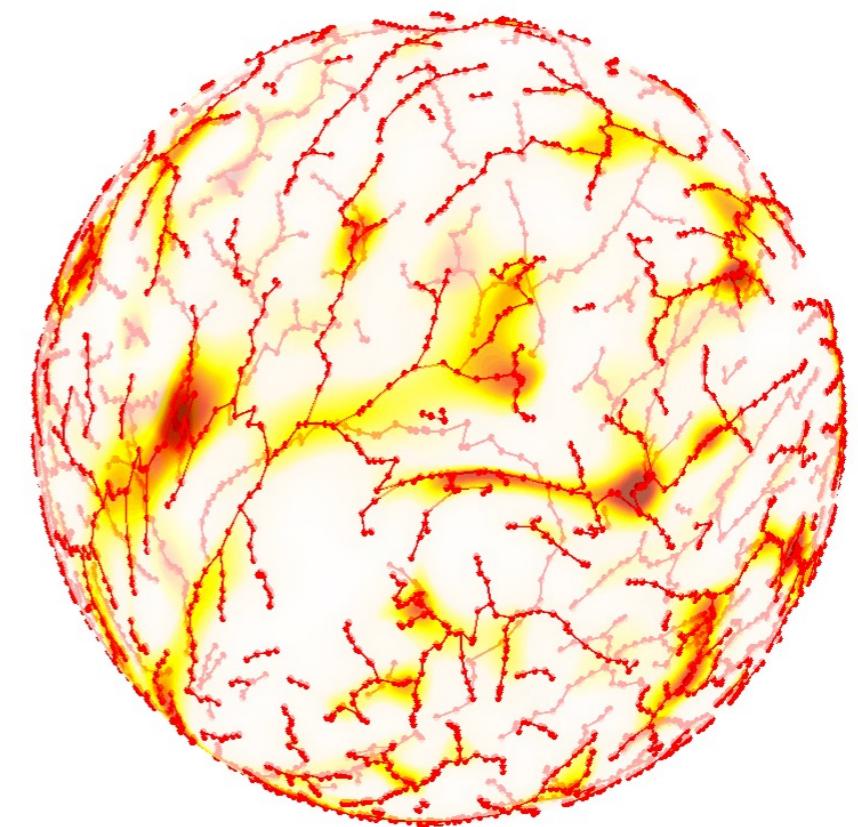
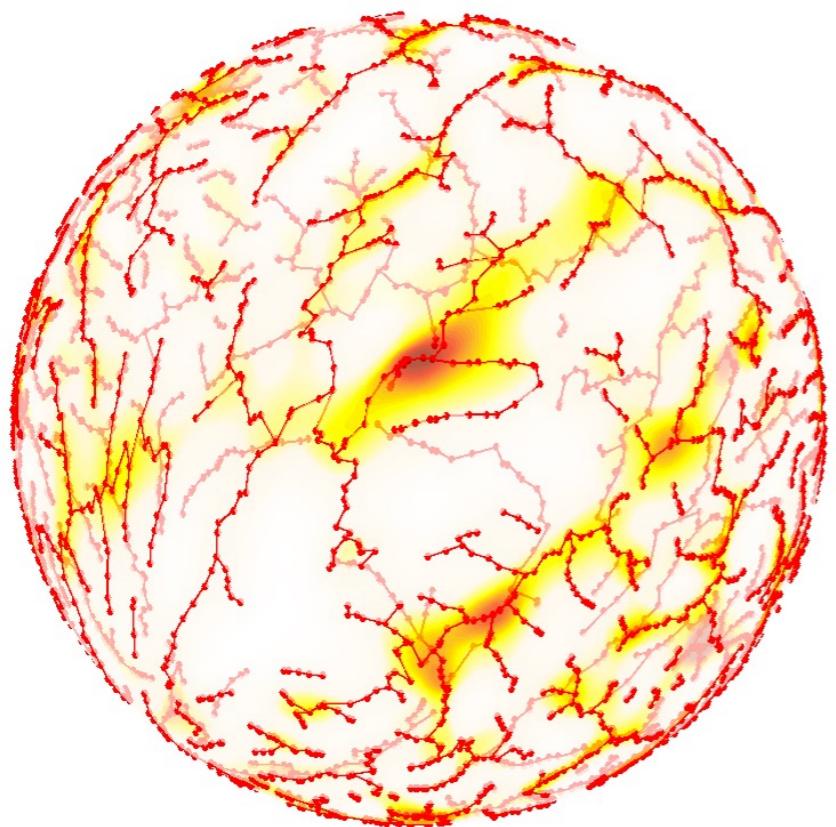
$$\mathcal{L}(P_1, P_2) = \inf_{\psi: P_1 \rightarrow P_2} \left(\sum_{x \in P_1} \|x - \psi(x)\|^2 \right)^{1/2}$$

Hungarian algorithm in $\mathcal{O}(q^3)$

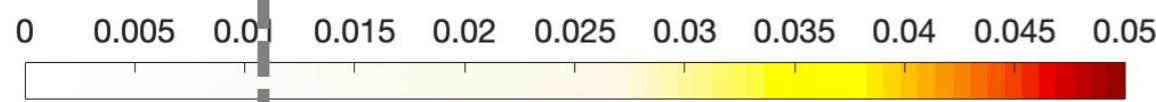
<https://github.com/laplcebeltrami/sulcaltree>



Theorem: Invariance of Wasserstein distance on heat kernel smoothing

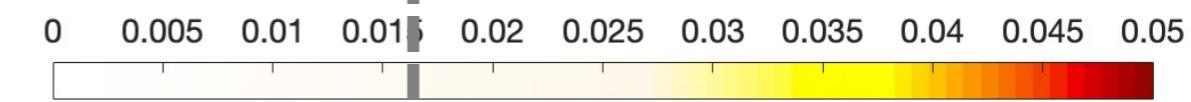


$$f_1(x) = \frac{1}{q} \sum_{i=1}^q \delta(x - x_i)$$



$$K_\sigma * f_1(x) = \frac{1}{q} \sum_{i=1}^q K_\sigma(x, x_i)$$

$$f_2(y) = \frac{1}{q} \sum_{i=1}^q \delta(y - y_i)$$



$$K_\sigma * f_2(y) = \frac{1}{q} \sum_{i=1}^q K_\sigma(y, y_i)$$

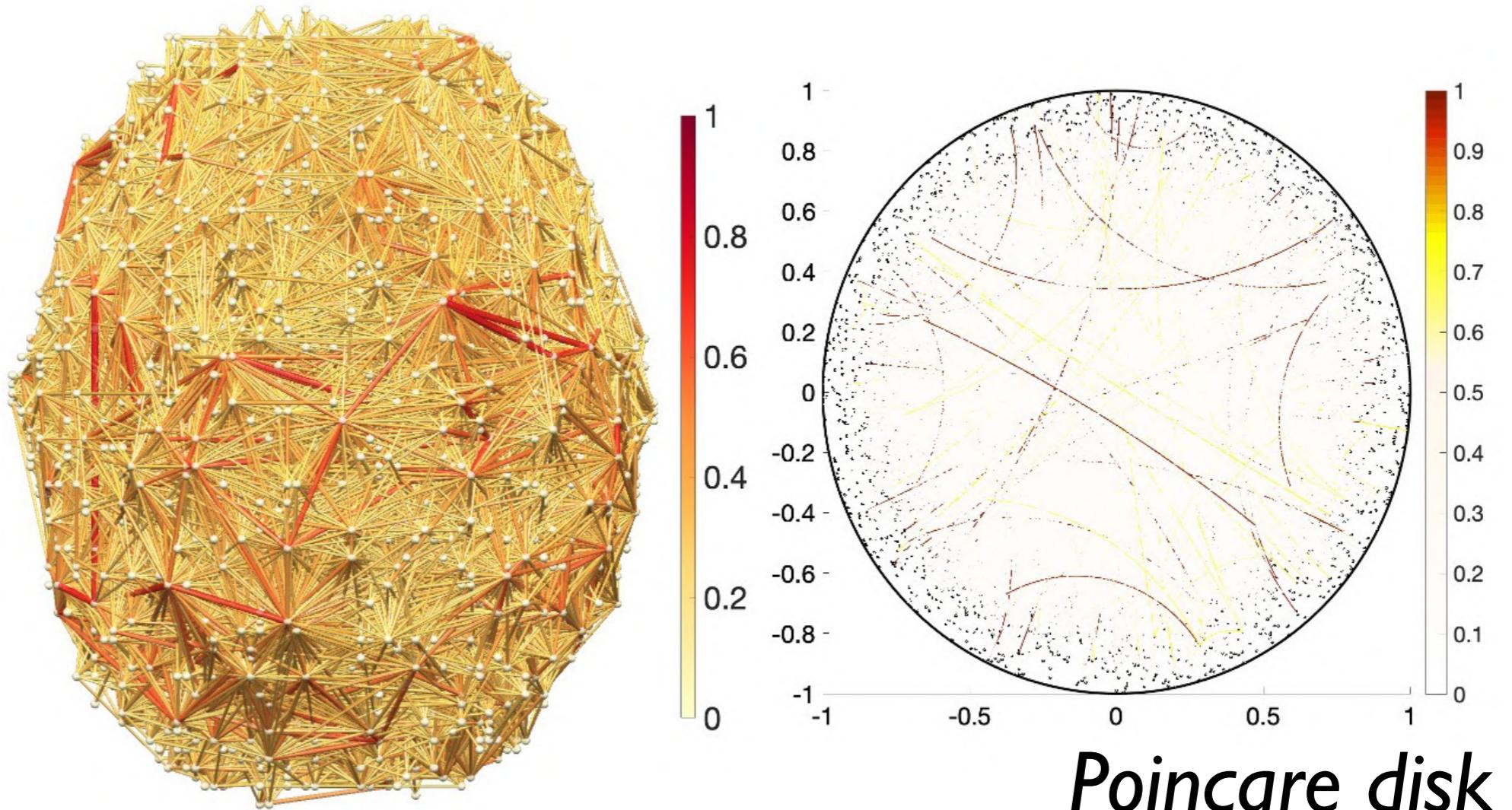
$$\mathcal{D}(f_1, f_2) = \mathcal{D}(K_\sigma * f_1, K_\sigma * f_2)$$

Chen et al. 2023 ISBI

Open research problem

Develop scalable algorithms for computing Wasserstein distance in other manifolds:

Space of positive definite symmetric matrices



Poincare disk

Theorem: Wasserstein distance on graph filtrations

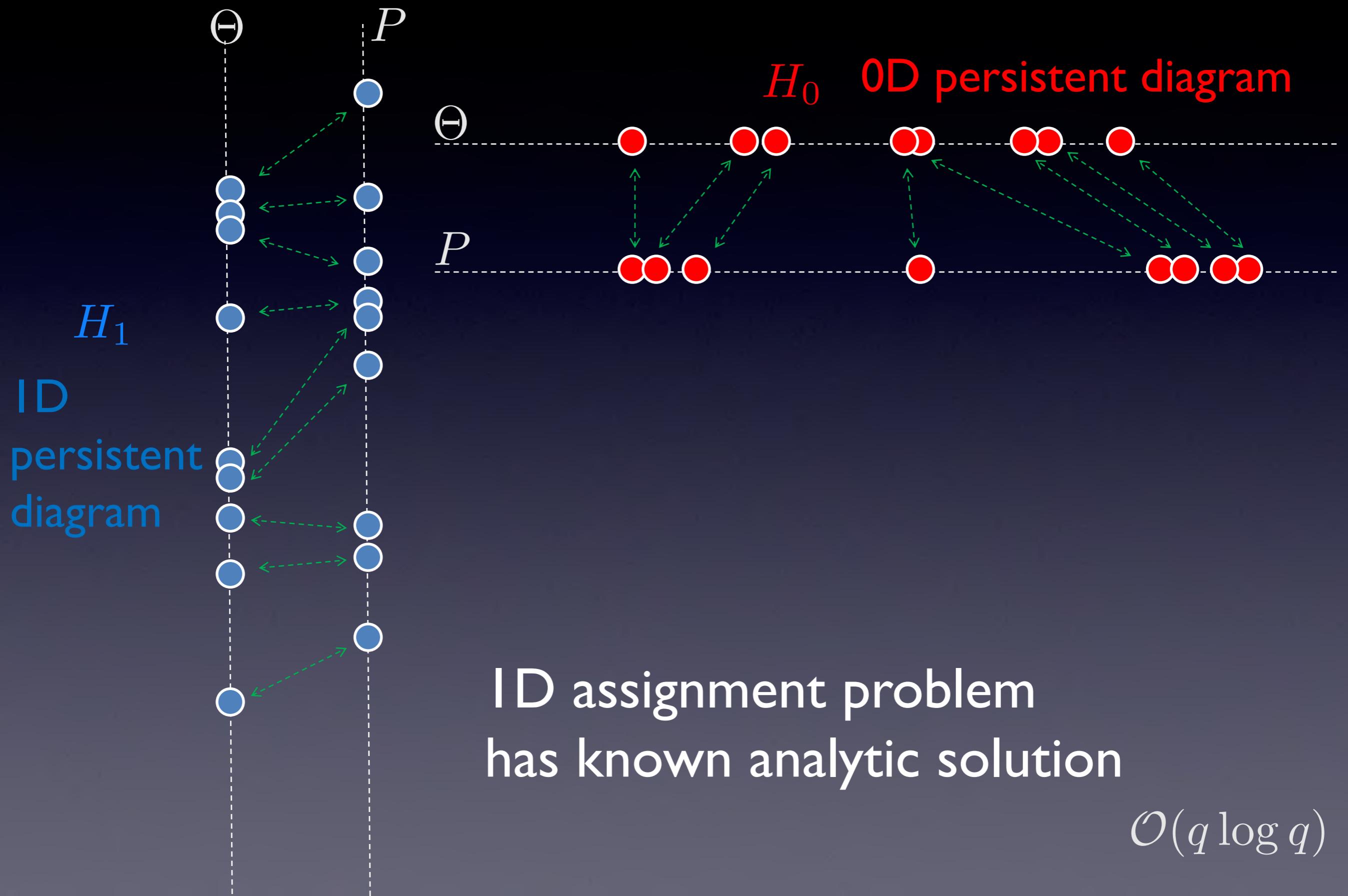
$$\begin{aligned}\mathcal{L}_{0D}(\Theta, P) &= \min_{\tau} \sum_{\substack{b \in E_0 \\ \text{Birth set}}} [b - \tau(b)]^2 \\ &= \sum_{\substack{b \in E_0}} [b - \tau_0^*(b)]^2\end{aligned}$$

τ_0^* :The i -th smallest birth value to the i -th smallest birth value

$$\begin{aligned}\mathcal{L}_{1D}(\Theta, P) &= \min_{\tau} \sum_{\substack{d \in E_1 \\ \text{Death set}}} [d - \tau(d)]^2 \\ &= \sum_{\substack{d \in E_1}} [d - \tau_1^*(d)]^2\end{aligned}$$

τ_1^* :The i -th smallest death value to the i -th smallest death value

Wasserstein distance for graph filtrations



Topological Inference *Clustering*

distance-based inference (our approach)

vs.

traditional feature-based inference

Ratio statistic for Wasserstein distances

$$C_1 \cup C_2 = \{\mathcal{X}_1, \dots, \mathcal{X}_n\}, \quad C_1 \cap C_2 = \emptyset$$

Between-group distance

$$l_B \propto \sum_{i \in C_1, j \in C_2} \mathcal{L}(\mathcal{X}_i, \mathcal{X}_j) \quad \text{<---- 0D, ID and combined distances}$$

Within-group distance

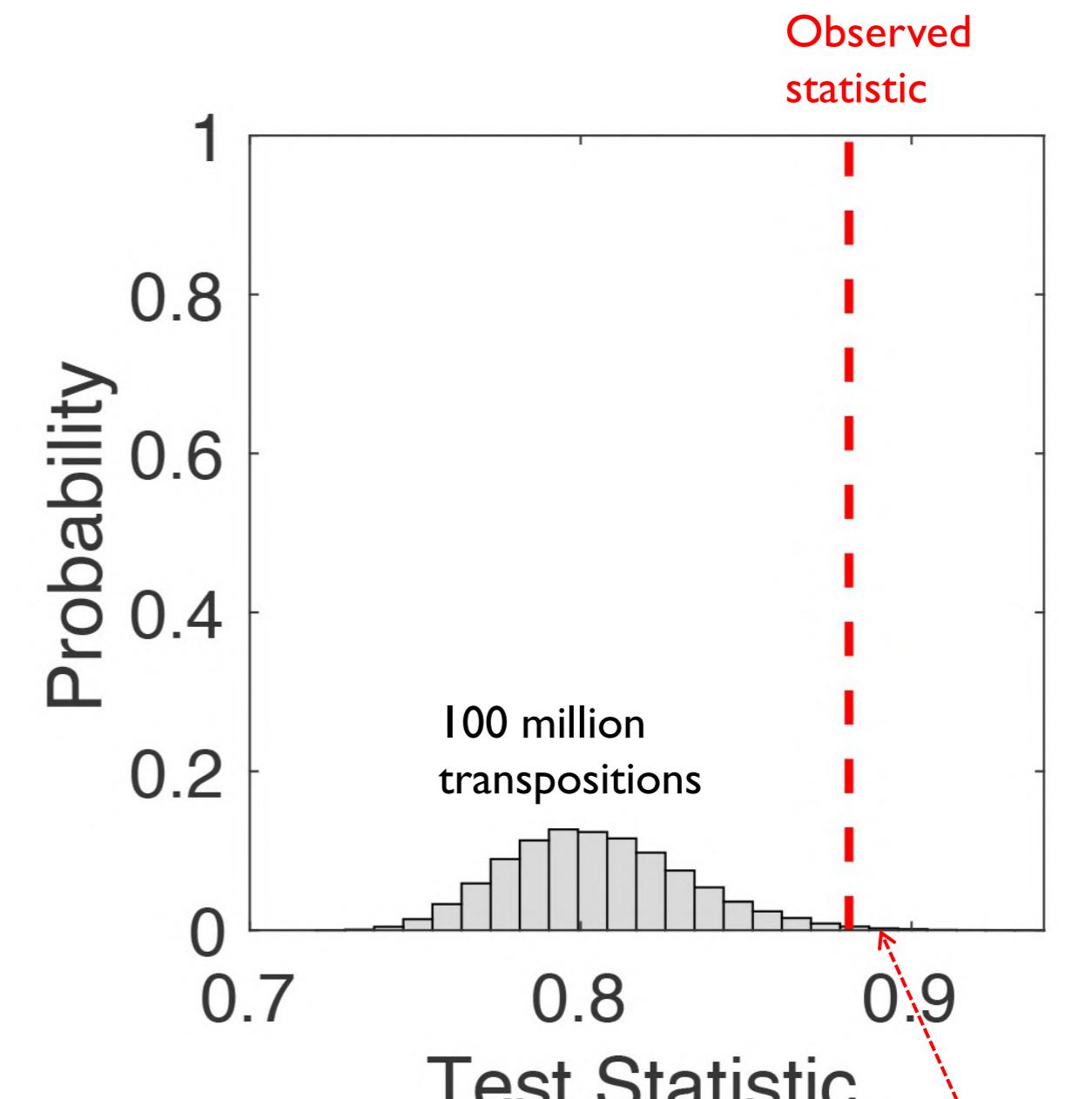
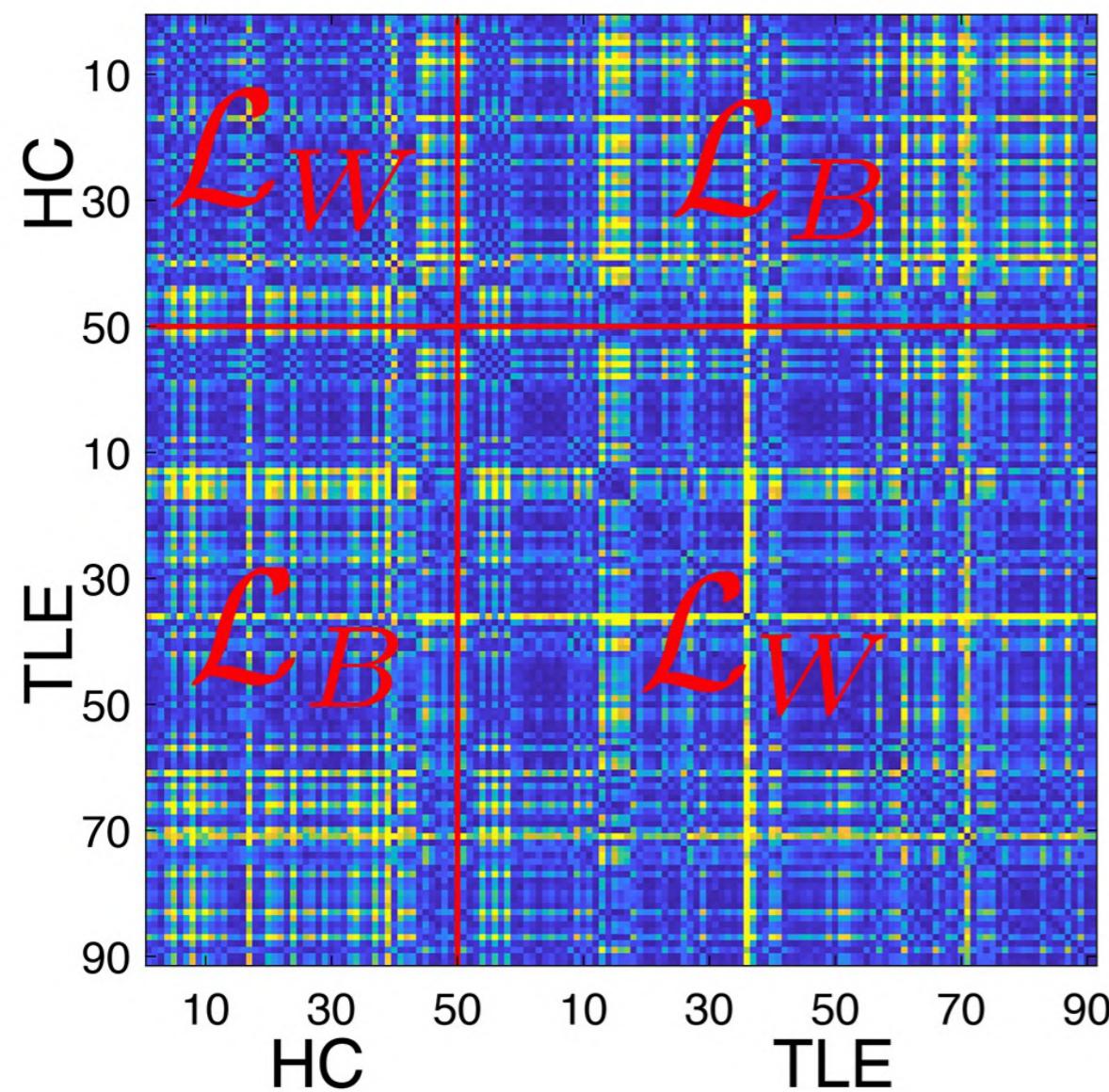
$$l_W \propto \sum_k \sum_{i, j \in C_k} \mathcal{L}(\mathcal{X}_i, \mathcal{X}_j) \quad \text{-----> Statistic} \quad \phi = \frac{l_B}{l_W}$$

Small $\phi \rightarrow$ small group separation

Large $\phi \rightarrow$ large group separation

*More complex
ANOVA-type
inference can
be easily done*

Online permutation test on pairwise distance matrix



$$l_W \rightarrow l_W + \Delta(\text{tranposition})$$

$$l_B \rightarrow l_B + \Delta(\text{tranposition})$$

Songdechakraiut and Chung 2023
Annals of Applied Statistics

P-value 0.0086

Topological clustering

$$C_1 \cup C_2 \cup \dots \cup C_k = \{\mathcal{X}_1, \dots, \mathcal{X}_n\}, \quad C_i \cap C_j = \emptyset$$

Minimize the within cluster distance

$$l_W \propto \sum_k \sum_{i,j \in C_k} \mathcal{L}(\mathcal{X}_i, \mathcal{X}_j)$$

Theorem: Topological clustering converges locally.

Algebraic proof: [arXiv: 2302.06673](https://arxiv.org/abs/2302.06673)

Geometric proof: [arXiv: 2201.00087](https://arxiv.org/abs/2201.00087)

Geometry of Wasserstein distance

Birth values are points in the convex polytope

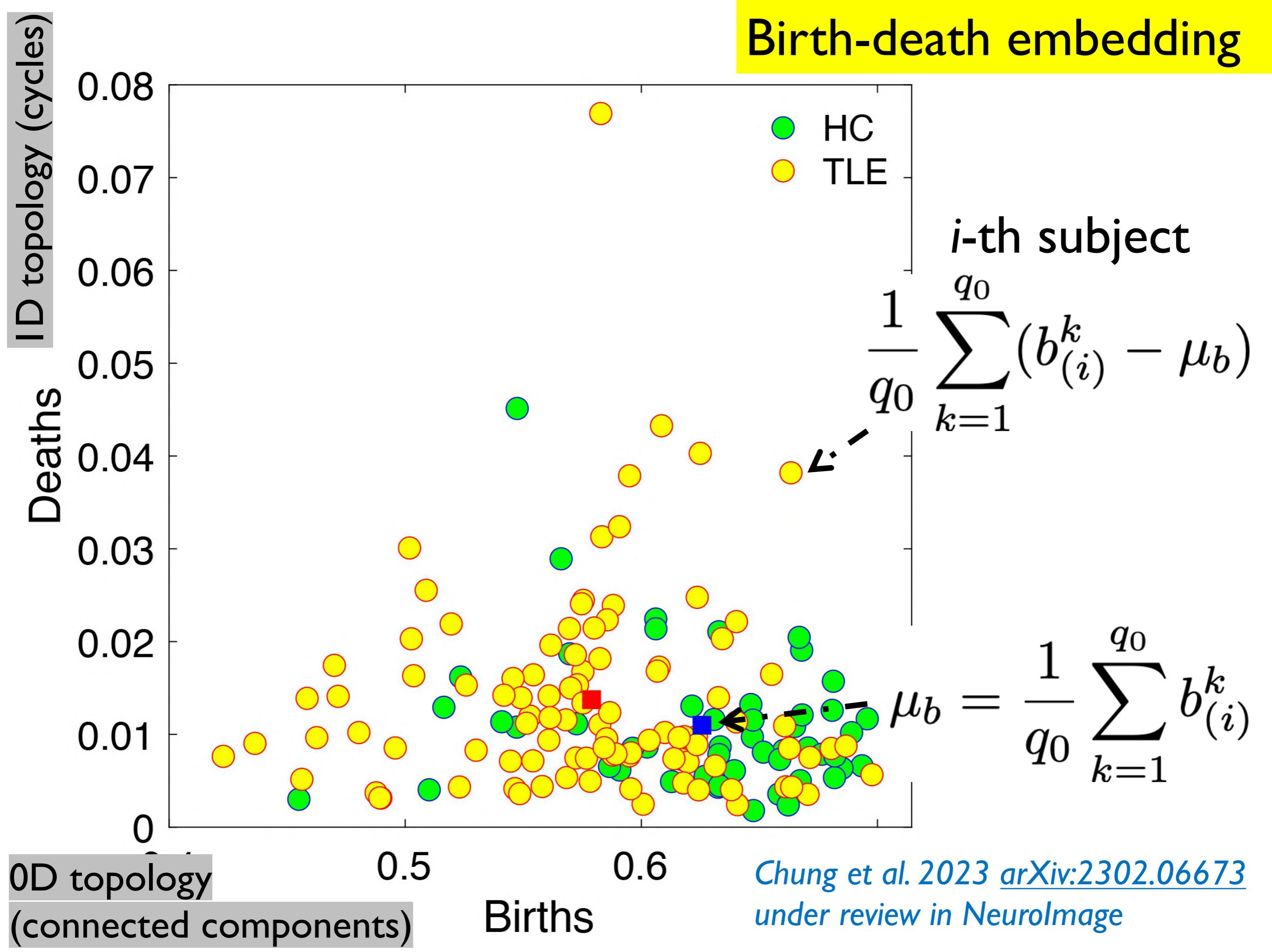
$$\mathcal{T}_0 = \{(x_1, x_2, \dots, x_{q_0}) \mid x_1 < x_2 < \dots < x_{q_0}\} \subset \mathbb{R}^{q_0}$$

Death values are points in the convex polytope

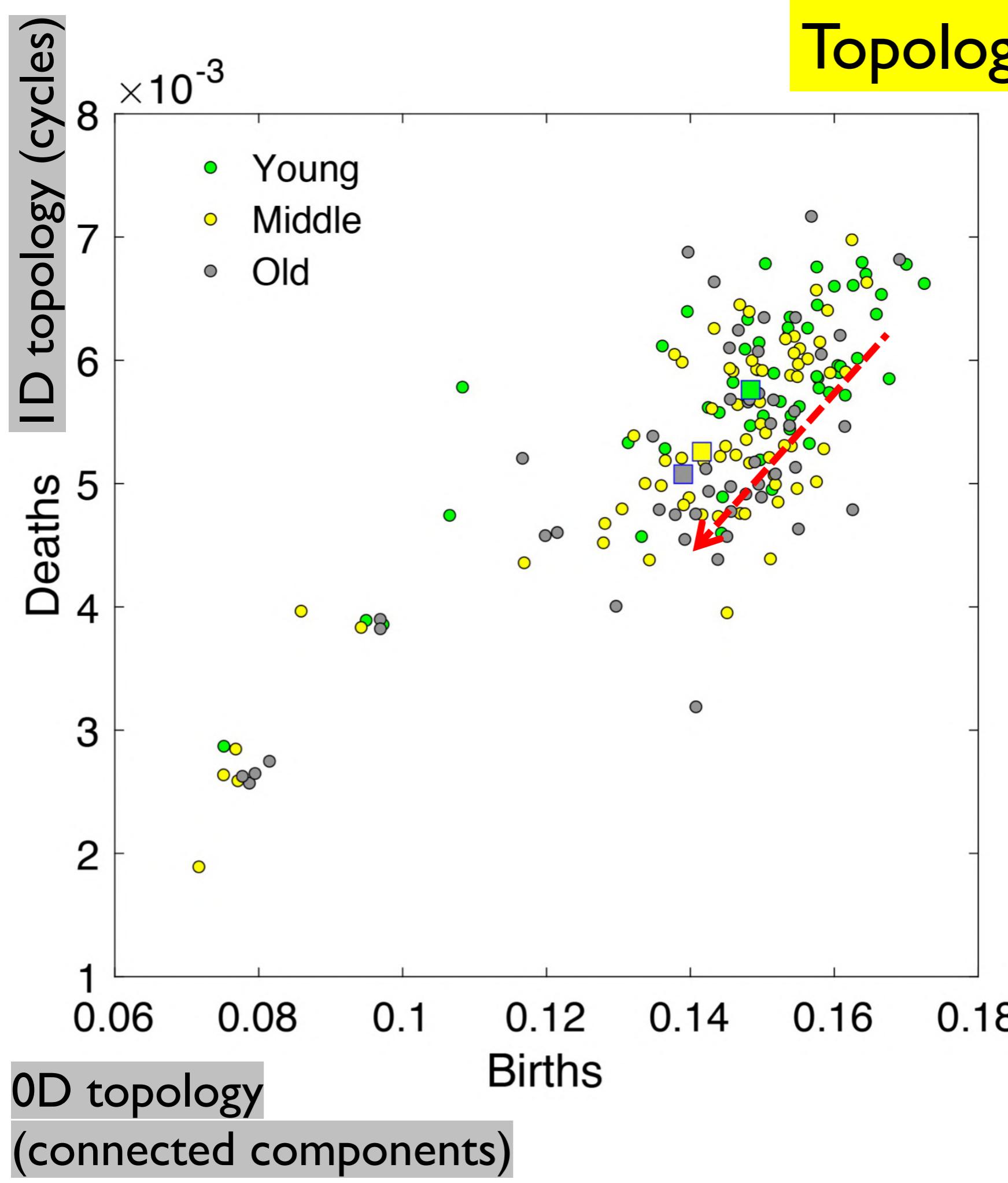
$$\mathcal{T}_1 = \{(x_1, x_2, \dots, x_{q_1}) \mid x_1 < x_2 < \dots < x_{q_1}\} \subset \mathbb{R}^{q_1}$$

The Wasserstein distance is equivalent to the Euclidean distance in the convex set $\mathcal{T}_0 \otimes \mathcal{T}_1$

Birth-death embedding



Topological gradient in aging



Decreasing birth
values →
more disconnected
subnetworks

Decreasing death
values →
cycles are disappearing

0D topology
(connected components)

Joint work with James Gee
of University of Pennsylvania

<https://github.com/laplcebeltrami/PH-STAT>

New simplicial complex data structure for brain networks

Structured/cell array can handle variable length data.

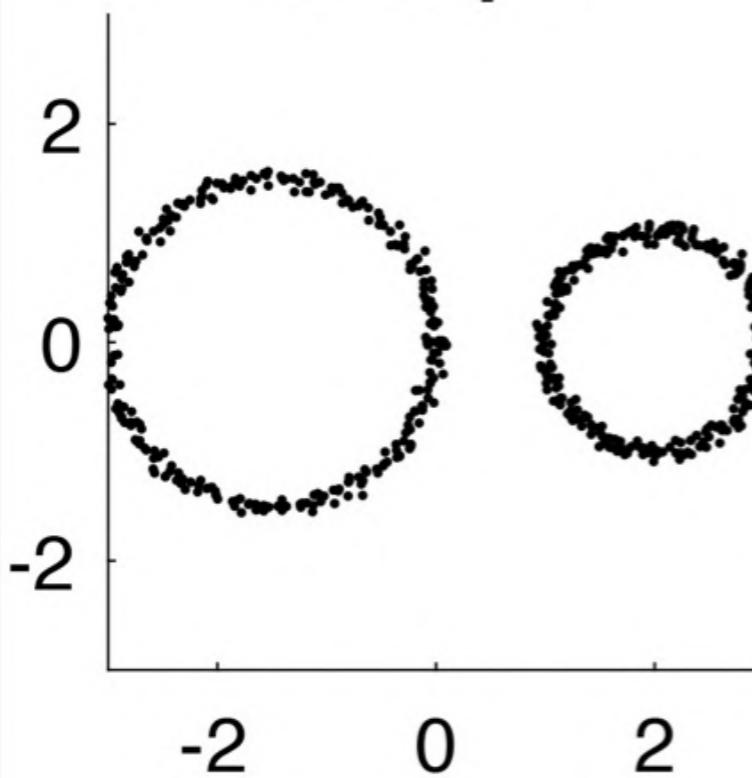
```
rng(2023); %fixed random seeds  
p=50; d=3; %p=# of nodes, d=dimension  
X = rand(p, d); %random in a cube  
radius = 0.3;  
S= PH_rips(X,d,radius) %Rips complex
```

Validation

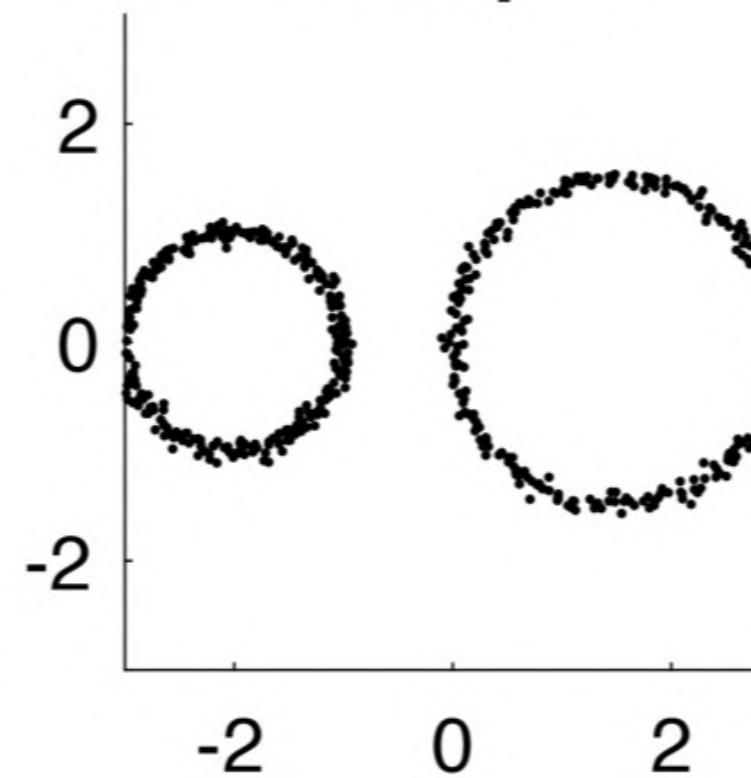
Testing if we are detecting topological false positives

$\sigma = 0.05$

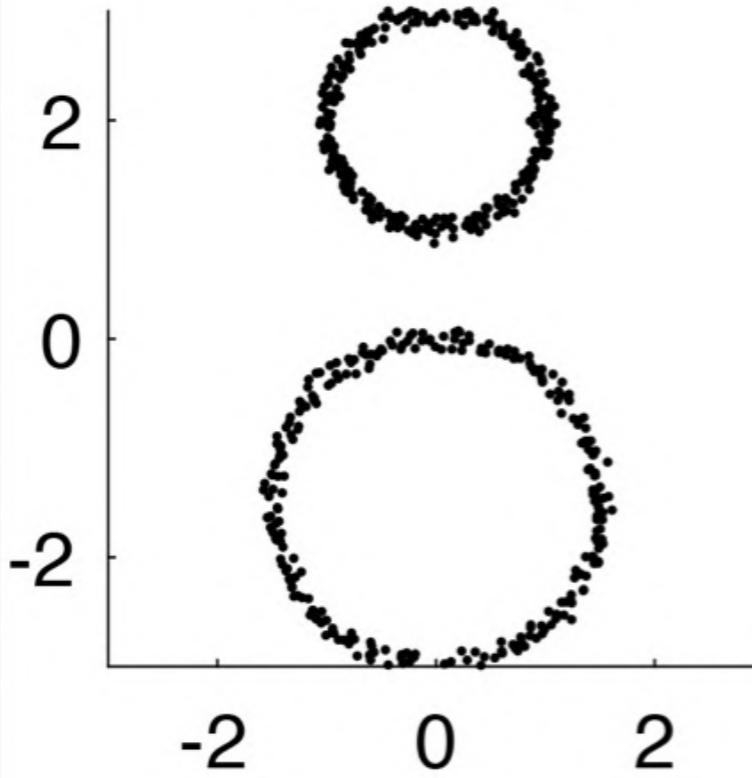
Group 1



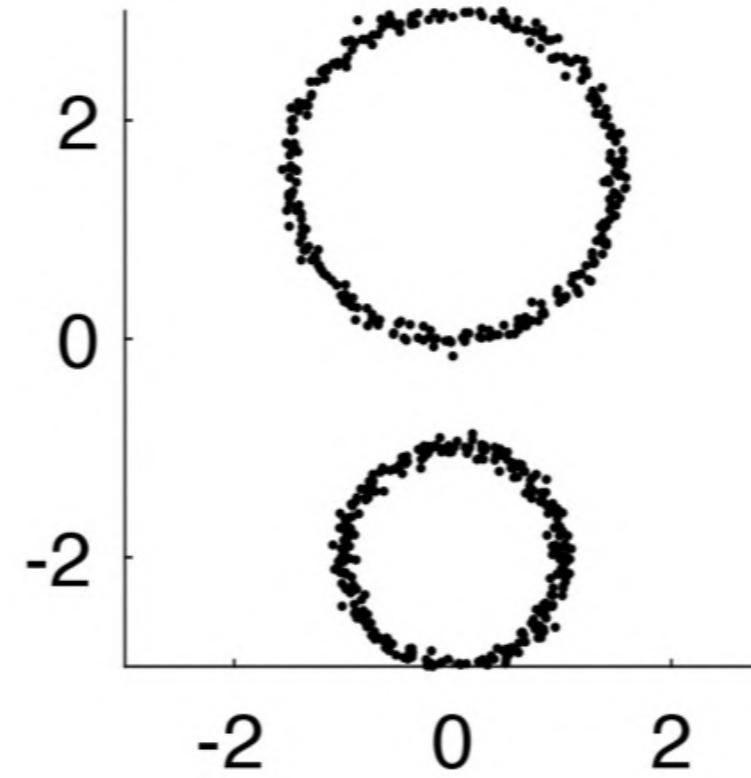
Group 2



Group 3



Group 4



All false positives

K-means
clustering

0.98 ± 0.01

Hierarchical
clustering

1.00 ± 0.00

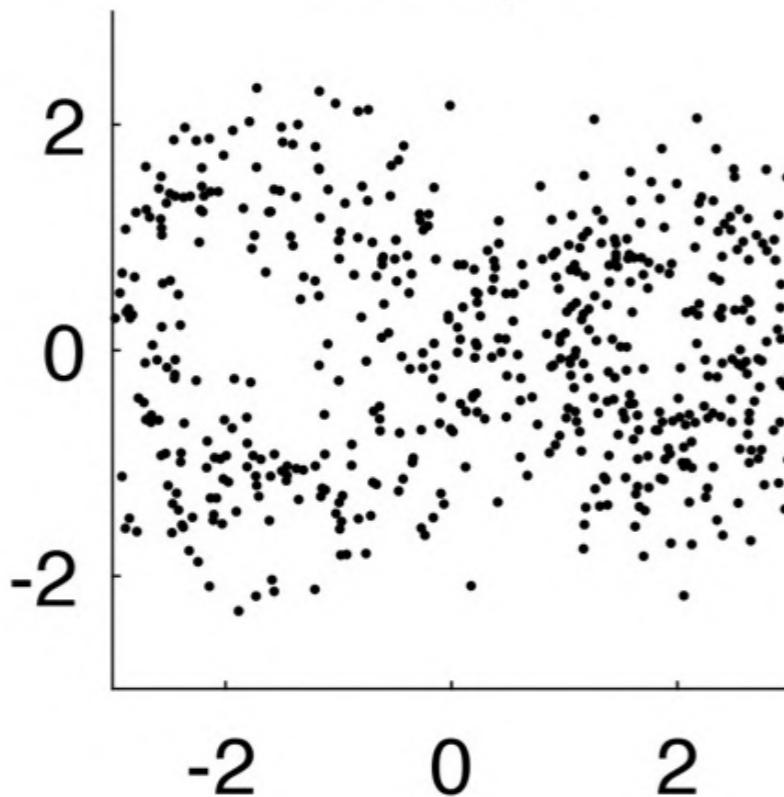
Topological
clustering

0.63 ± 0.04

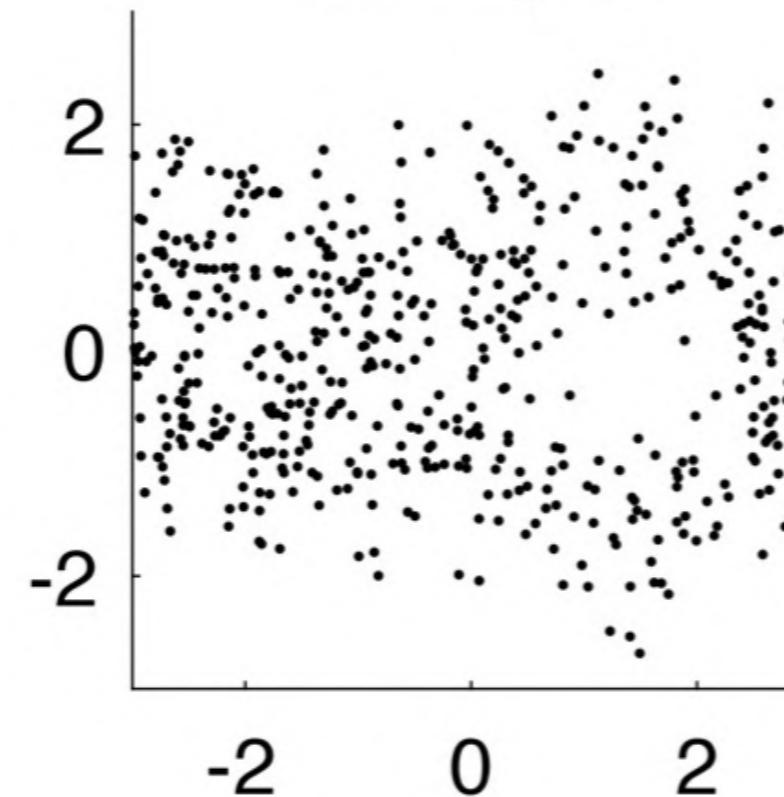
Testing if we are detecting topological false positives

$\sigma = 0.5$

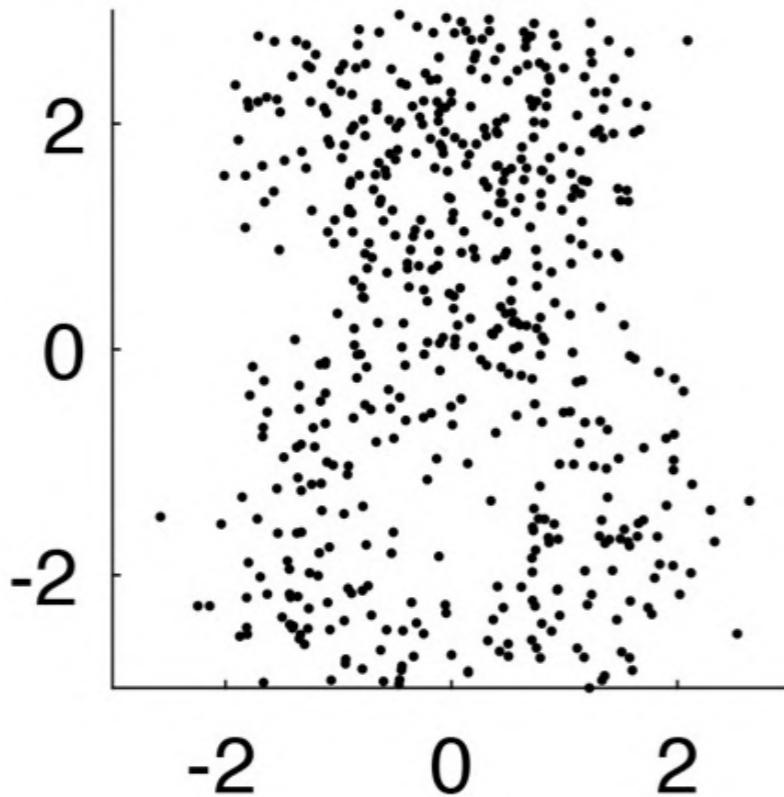
Group 1



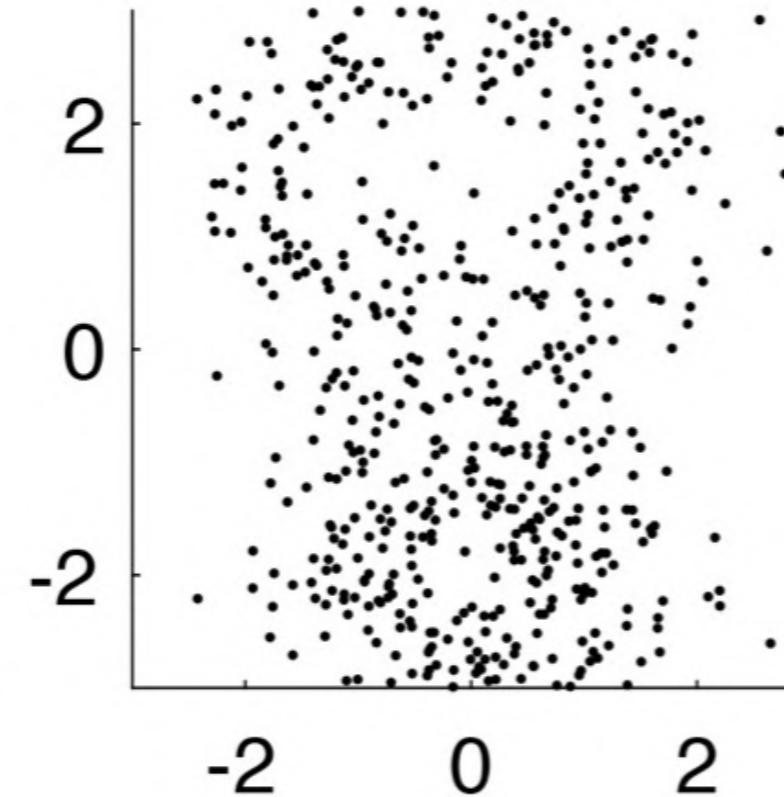
Group 2



Group 3



Group 4



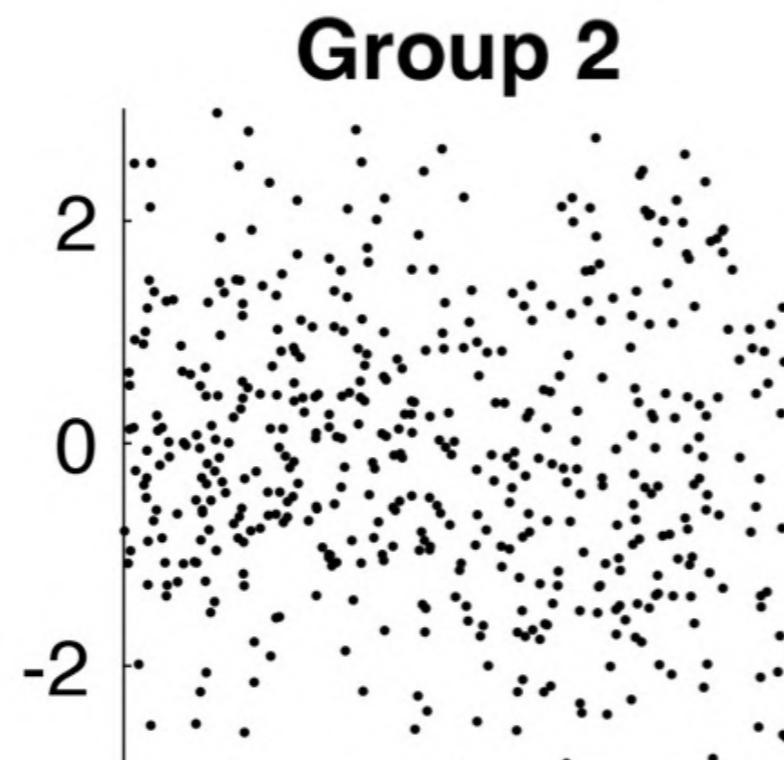
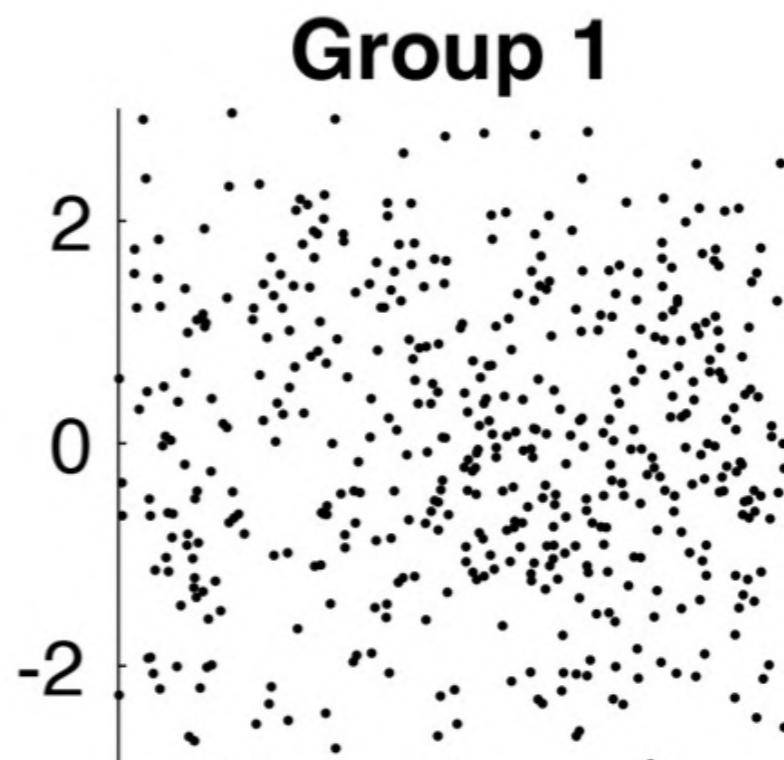
K-means
clustering
0.81 +/- 0.02

Hierarchical
clustering
1.00 +/- 0.00

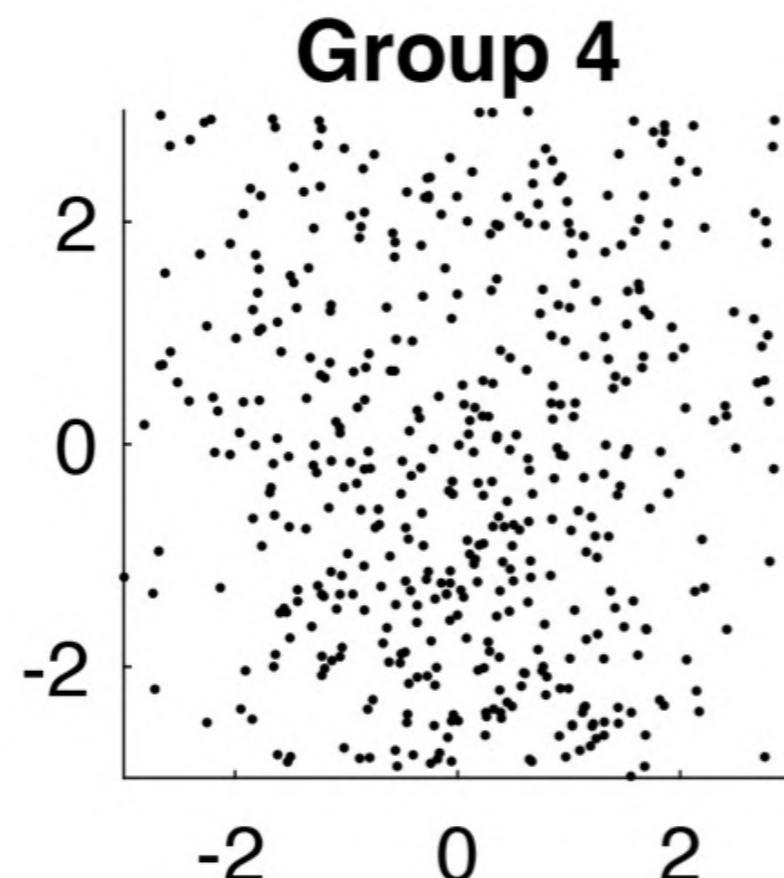
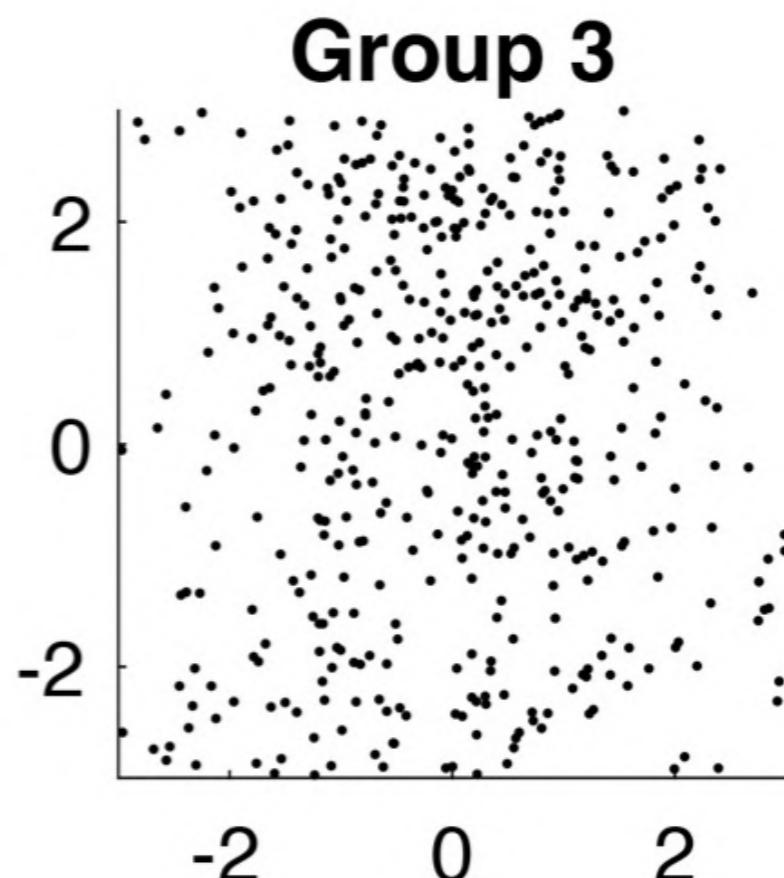
Topological
clustering
0.44 +/- 0.04

Testing if we are detecting topological false positives

$\sigma = 1.0$



K-means
clustering
0.70 +/- 0.02



Hierarchical
clustering
0.91 +/- 0.08

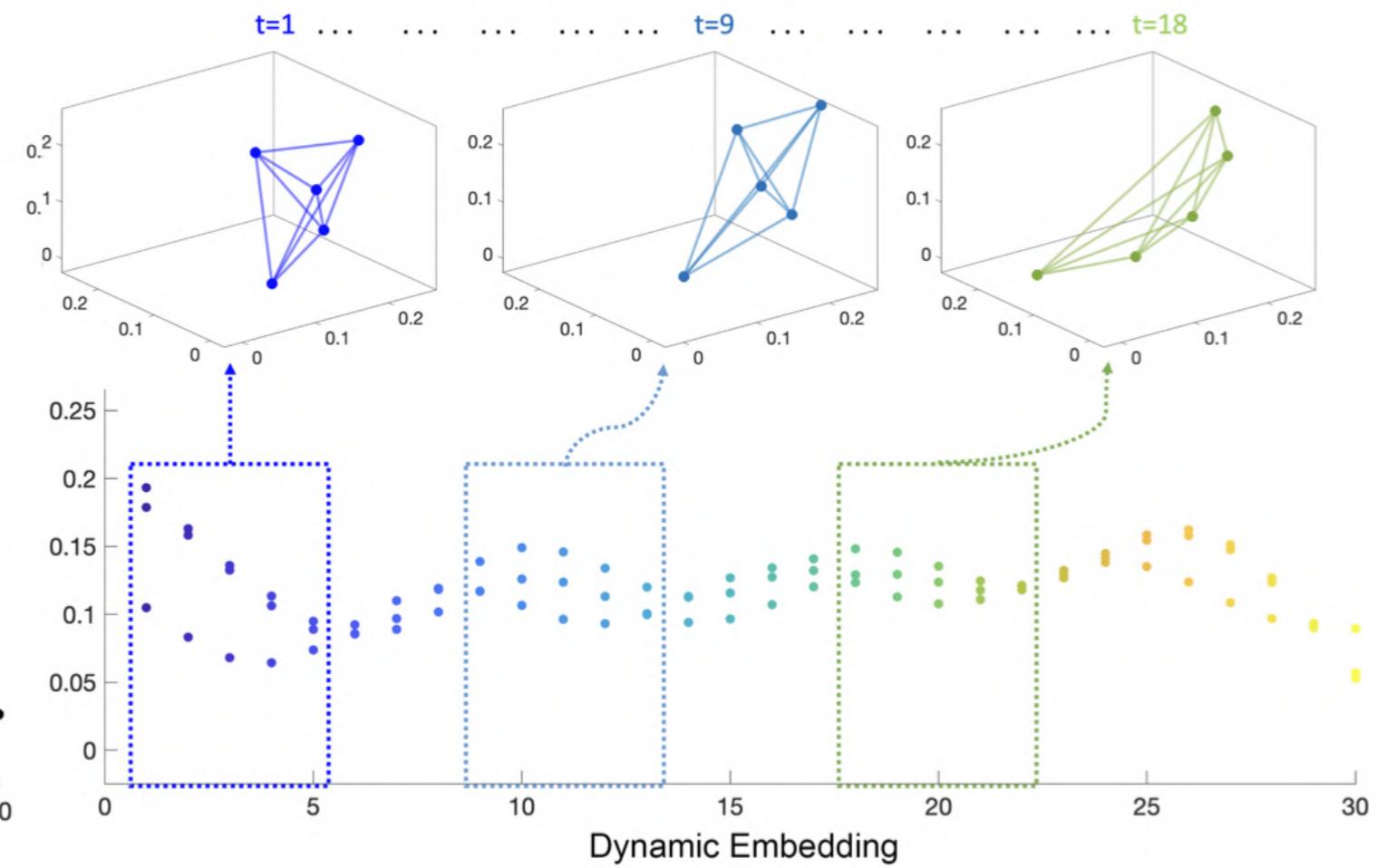
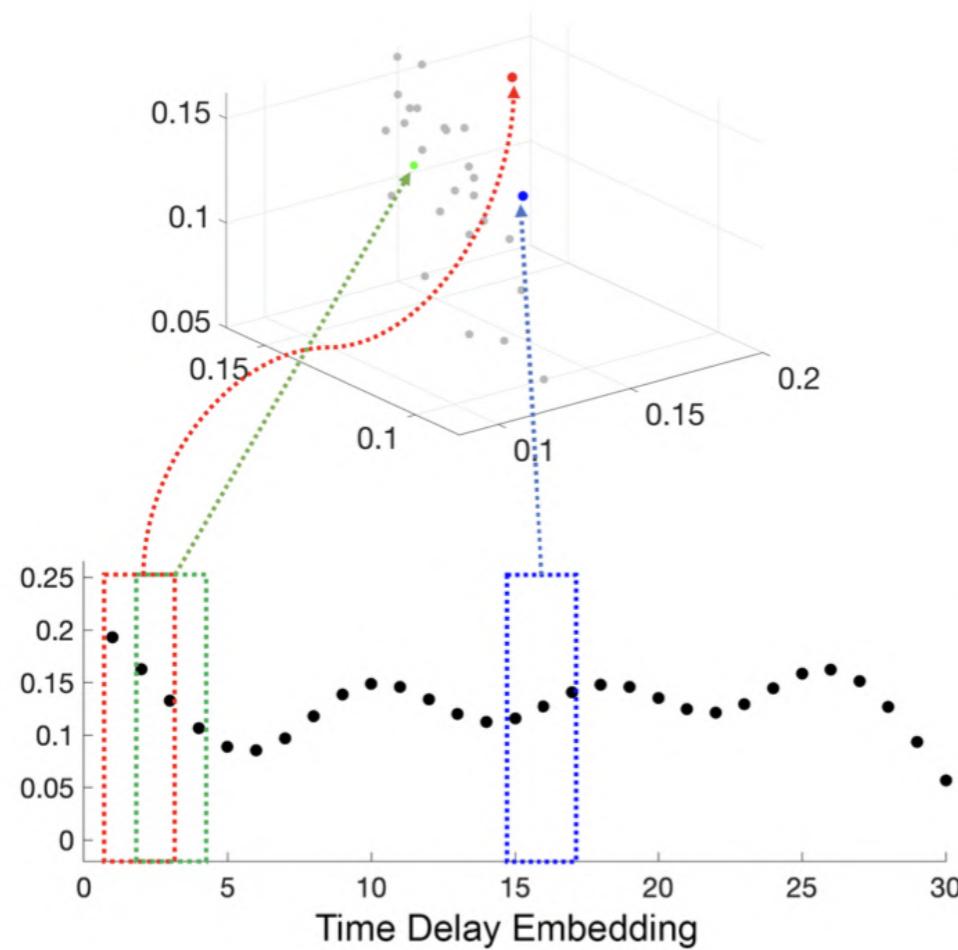
Topological
clustering
0.43 +/- 0.04

Results

Open research problem: Embedding of time series data

6

SOUMYA DAS, HERNANDO OMBAO, MOO K. CHUNG

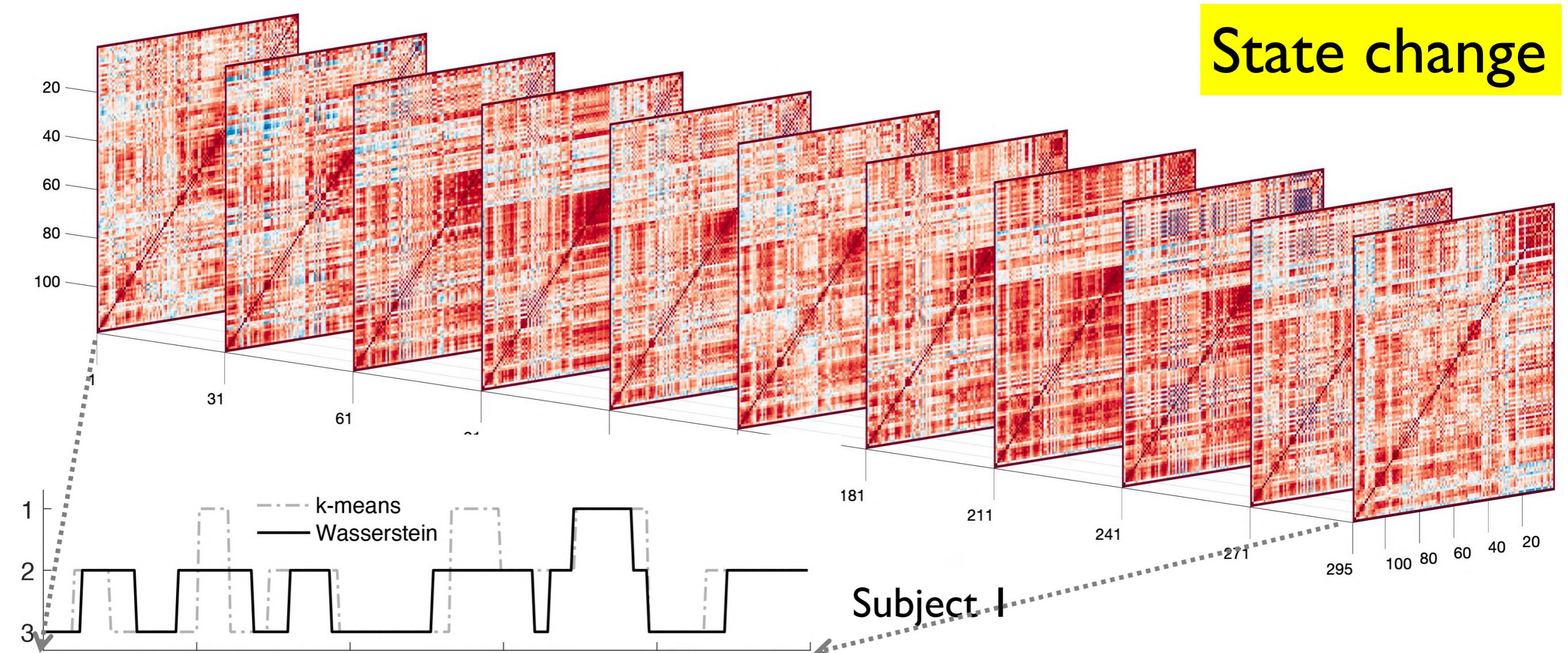


Das et al. 2022 arXiv:2210.09092

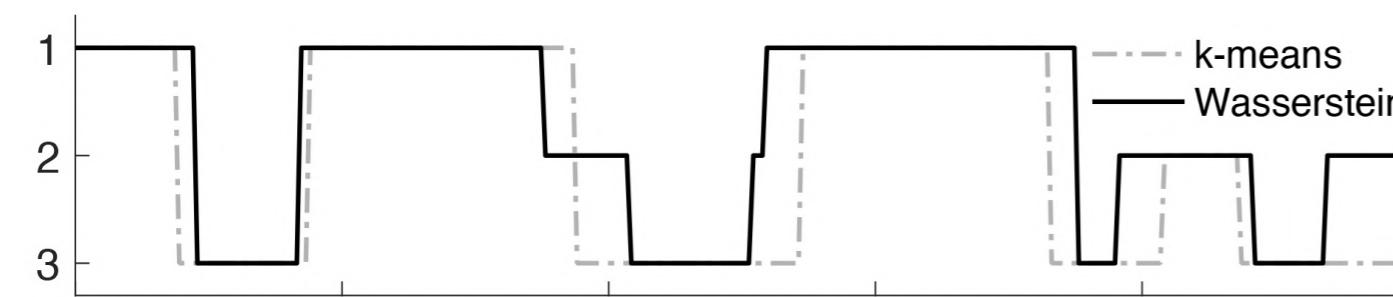
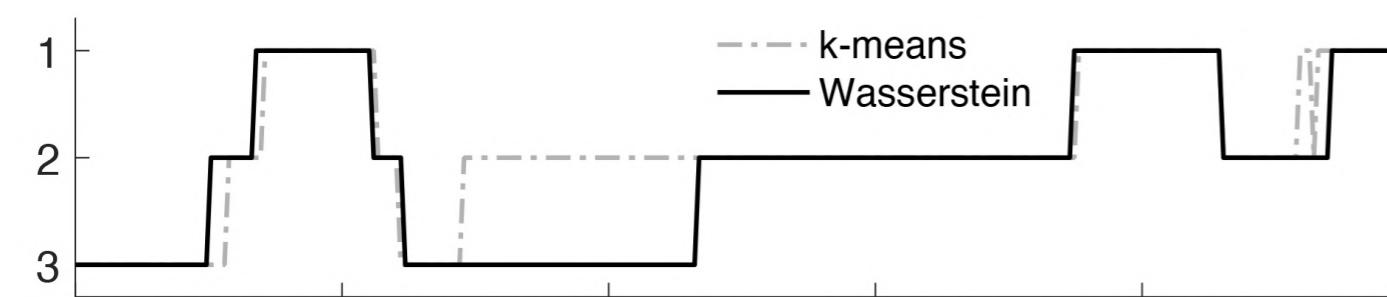
Under review in [Foundations of Data Science](#)

Journal has the heaviest concentration of TDA experts in the editorial board

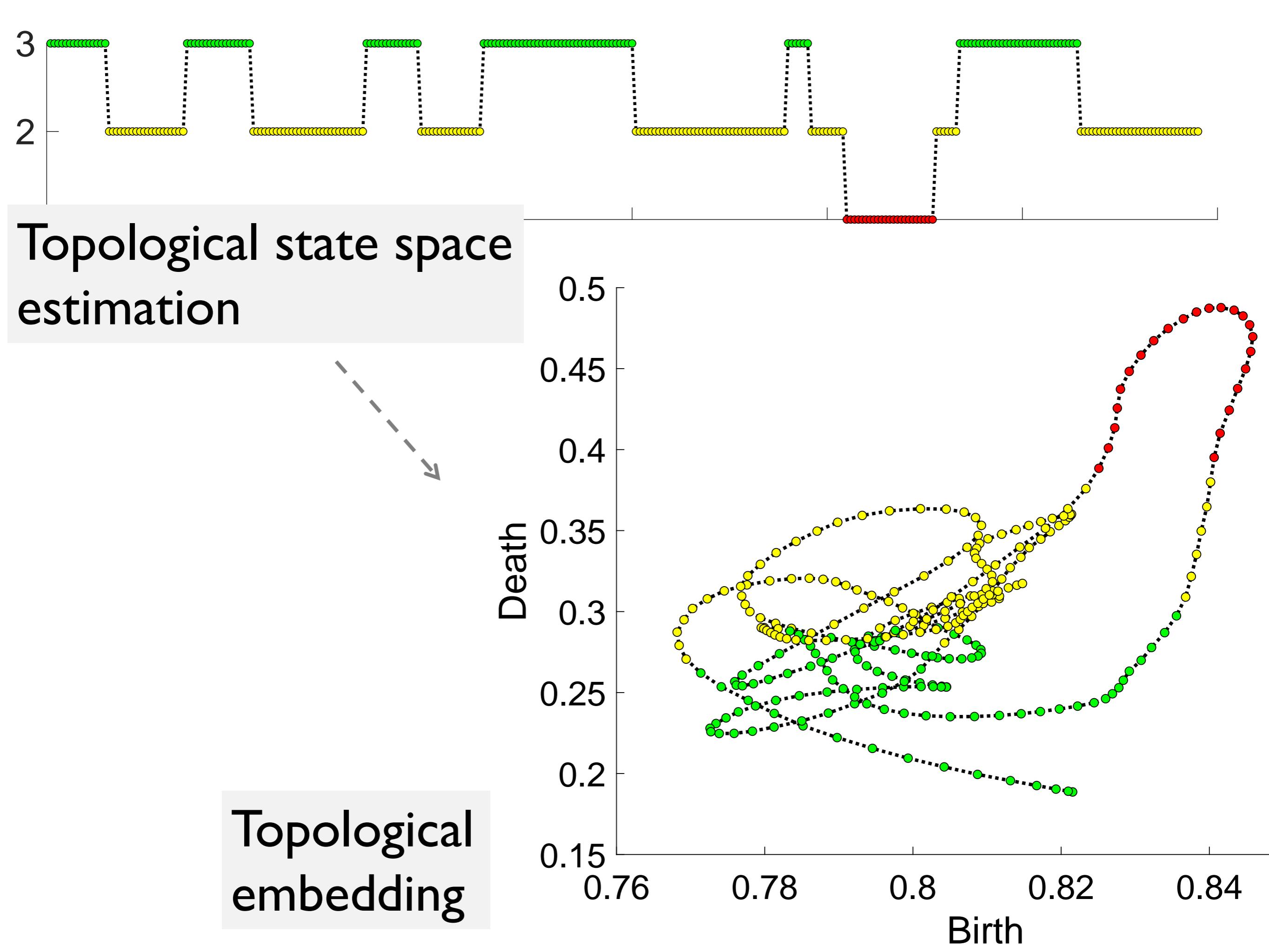
State change



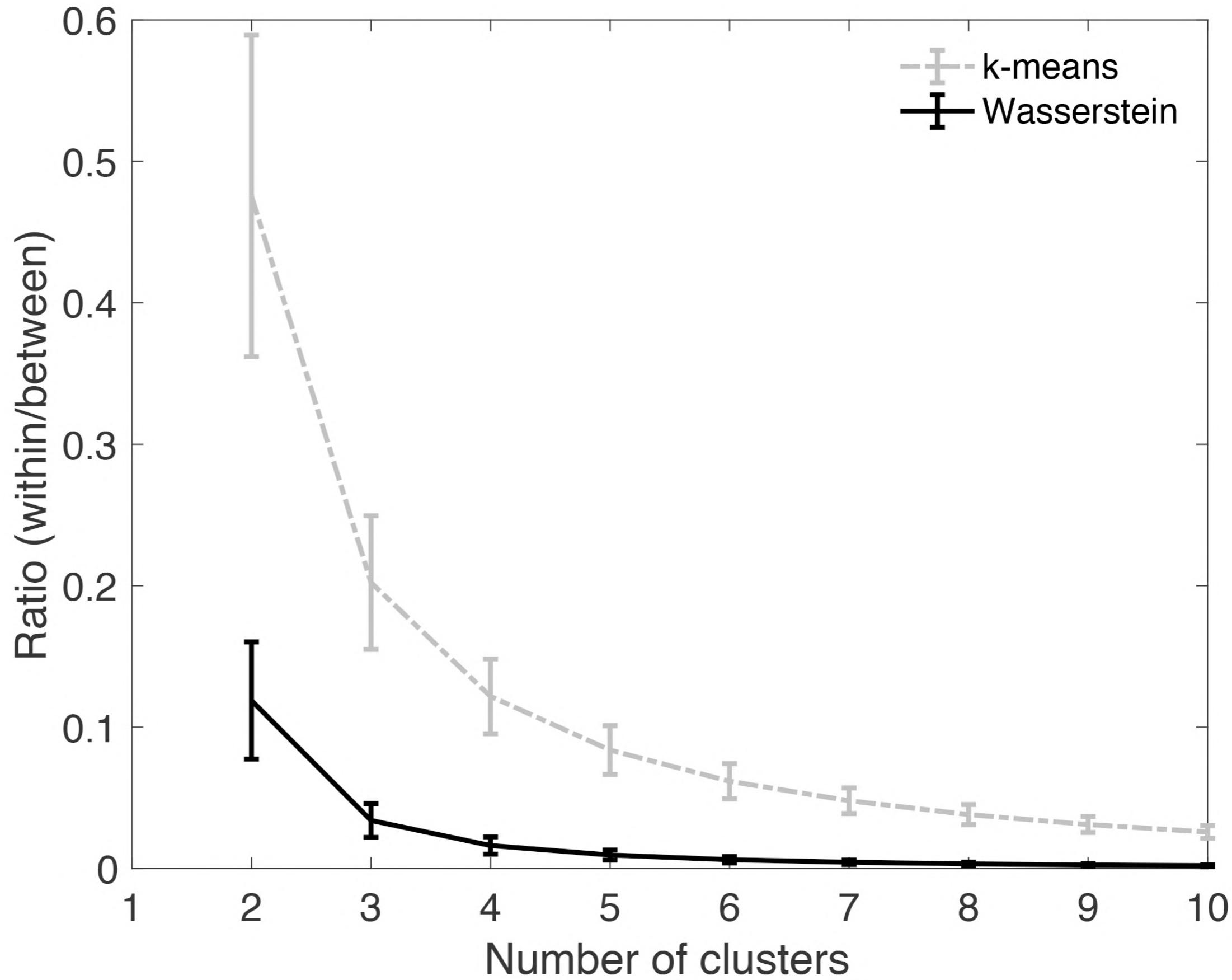
Clustering on
479 subjects



UW-Madison
Twin study

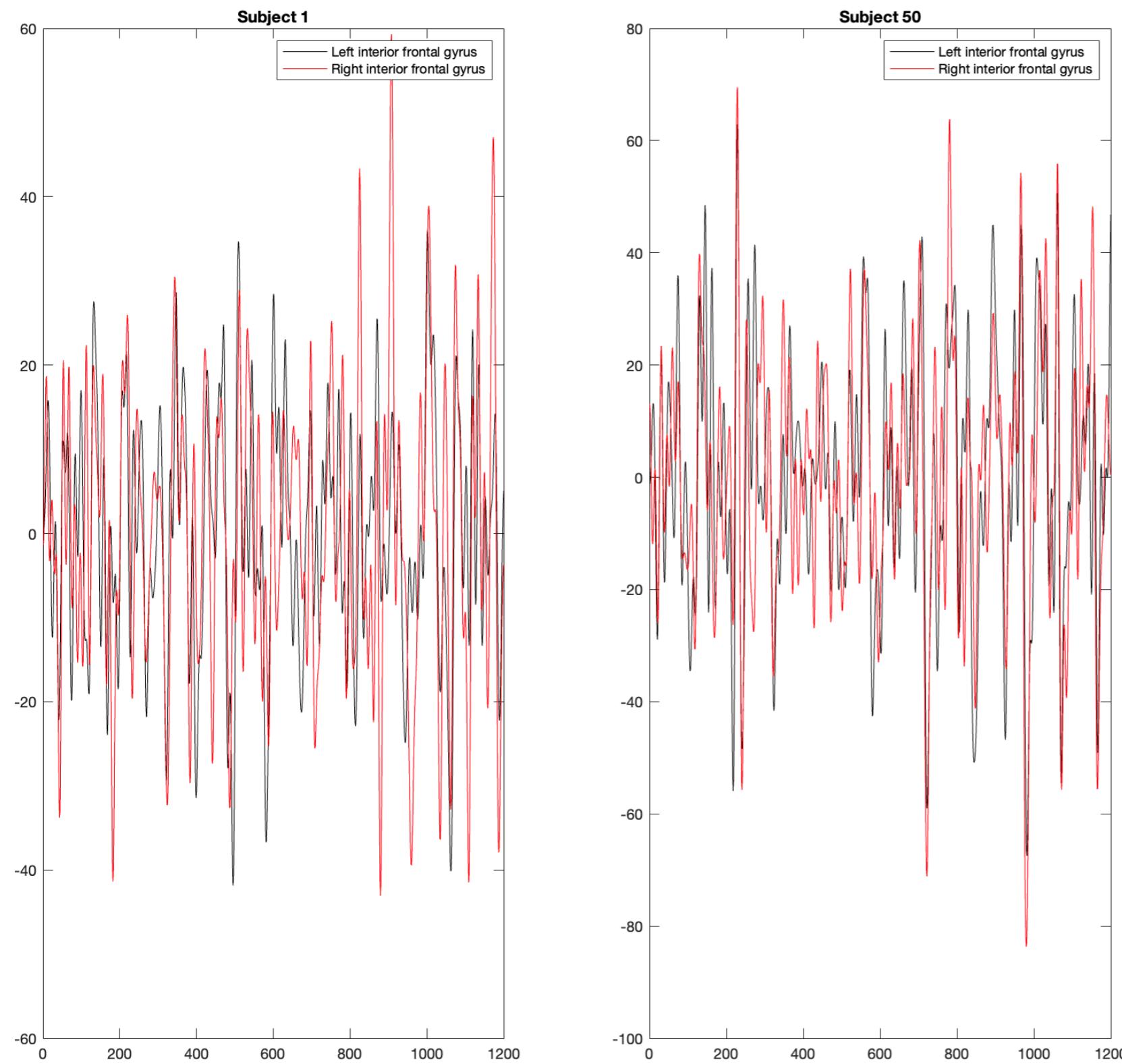


$$\frac{1}{\phi} = \frac{l_W}{l_B}$$



The within cluster variance **6 times** smaller

Open research problem

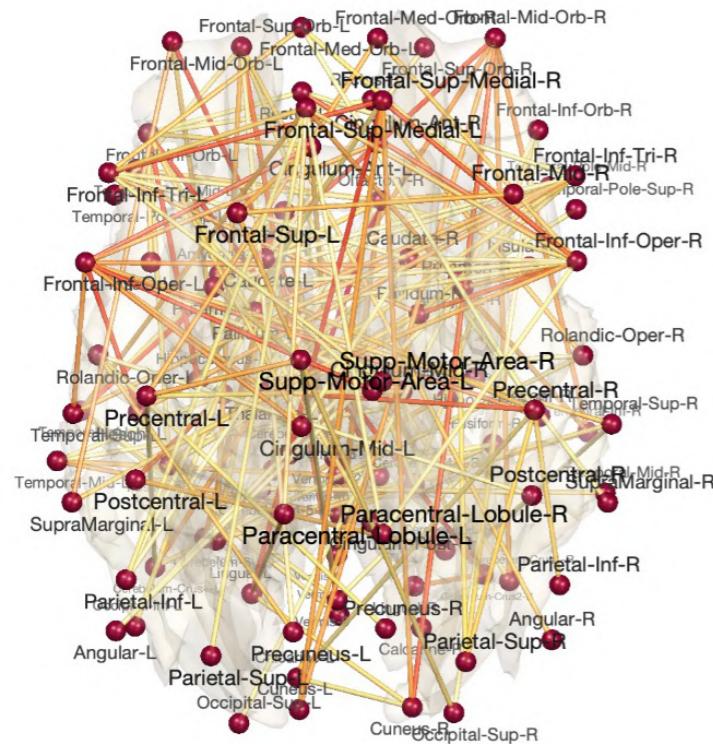


How to do a joint clustering of paired time series?

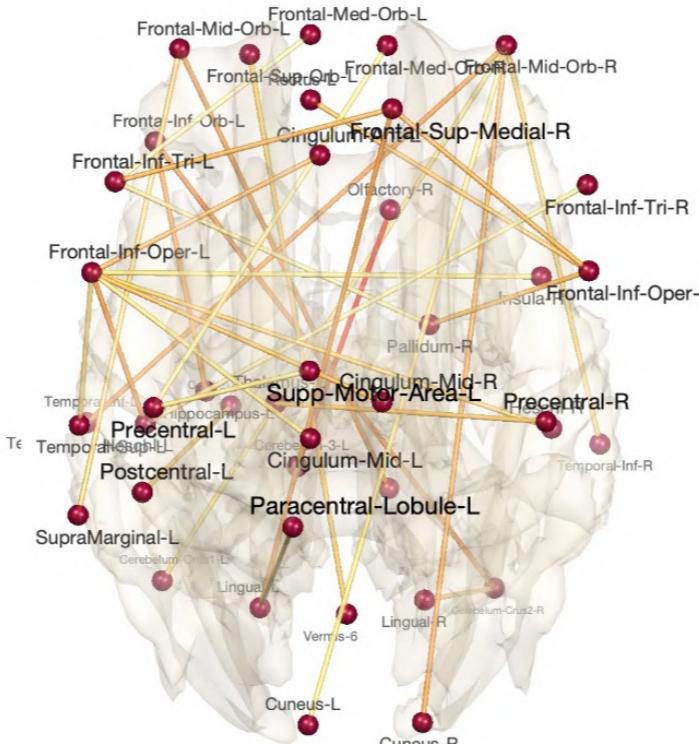
Is the estimated state space periodic?

How to cluster such that we decompose signals into periodic and nonperiodic parts

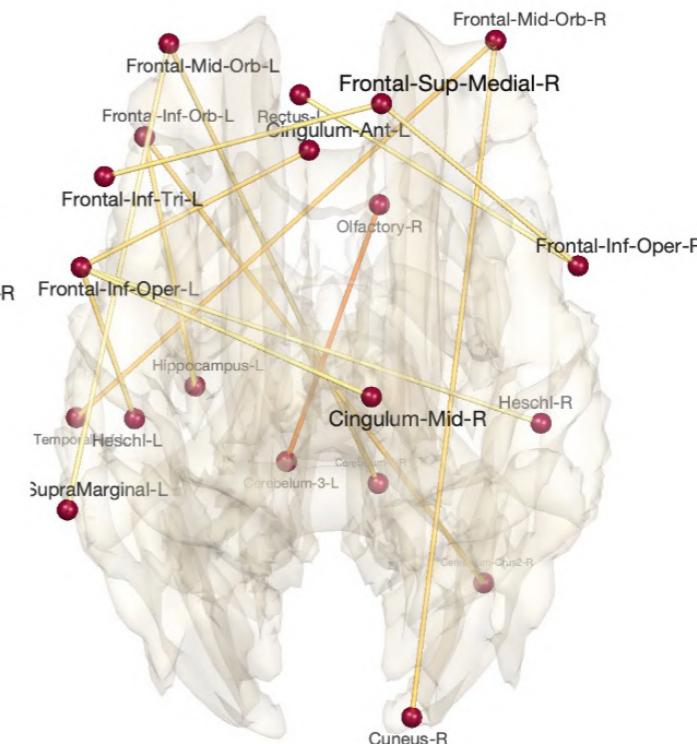
State 1



State 2

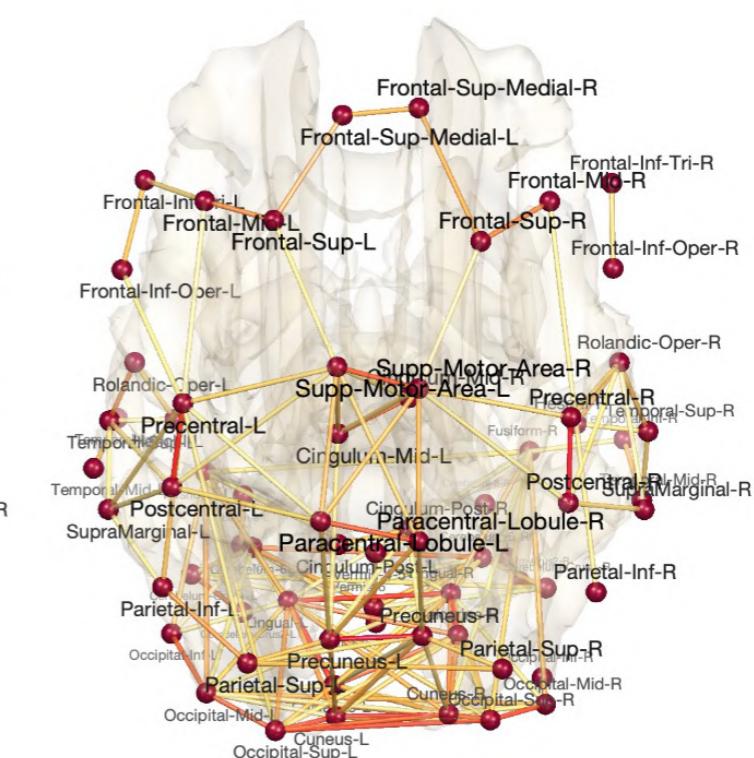
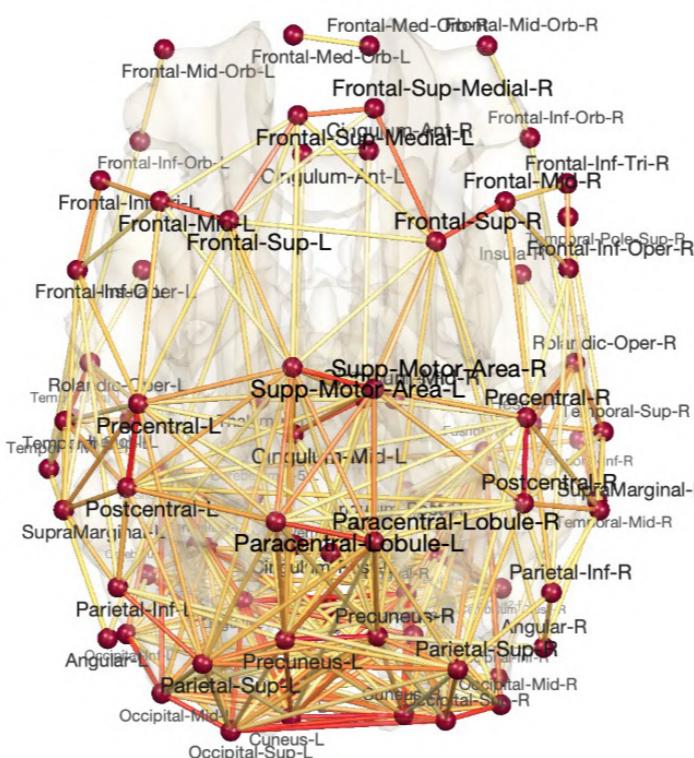
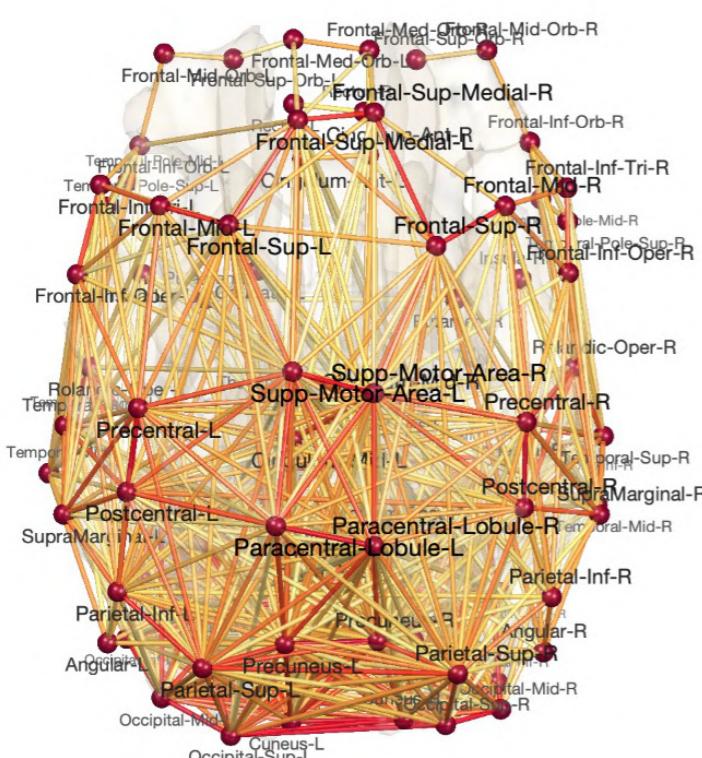


State 3



k-means

Sample mean in each state

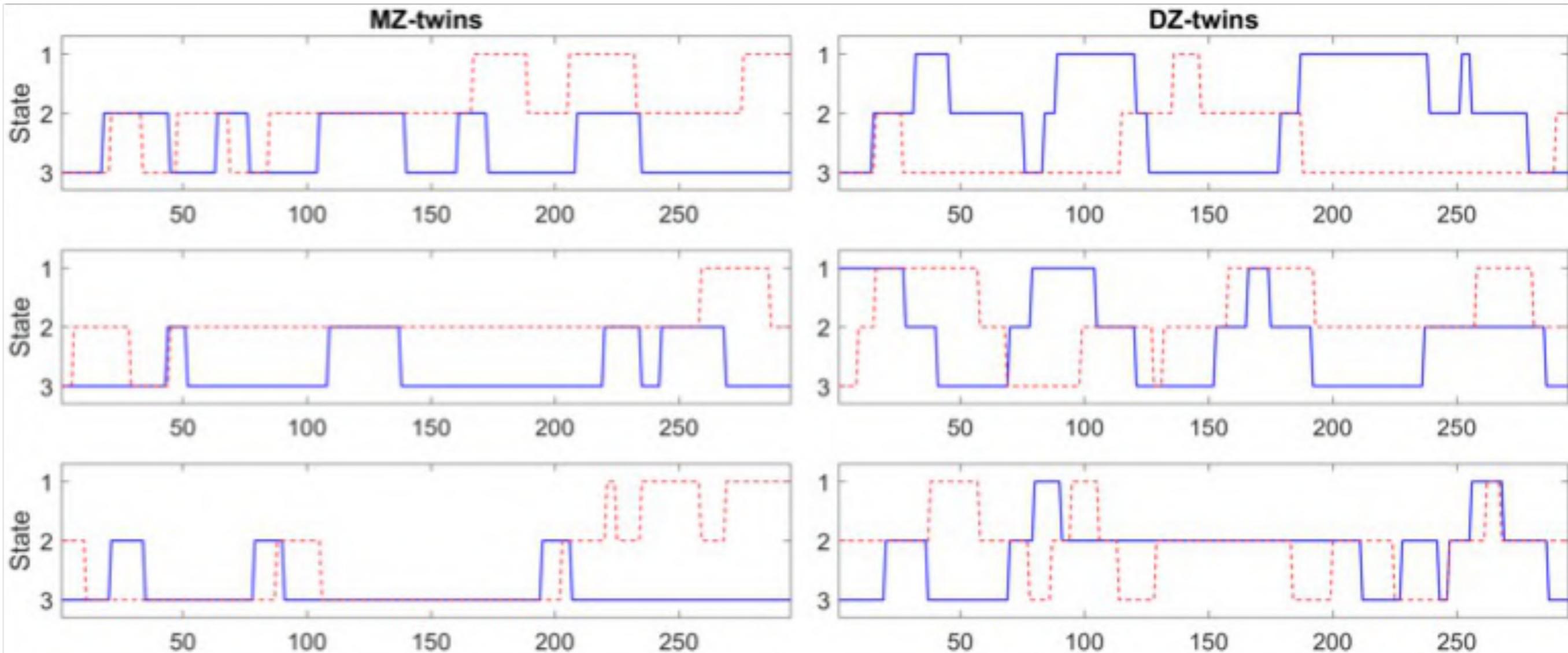


Wasserstein

Topological mean in each state

State space estimation on 479 subjects

Is the state-change heritable?

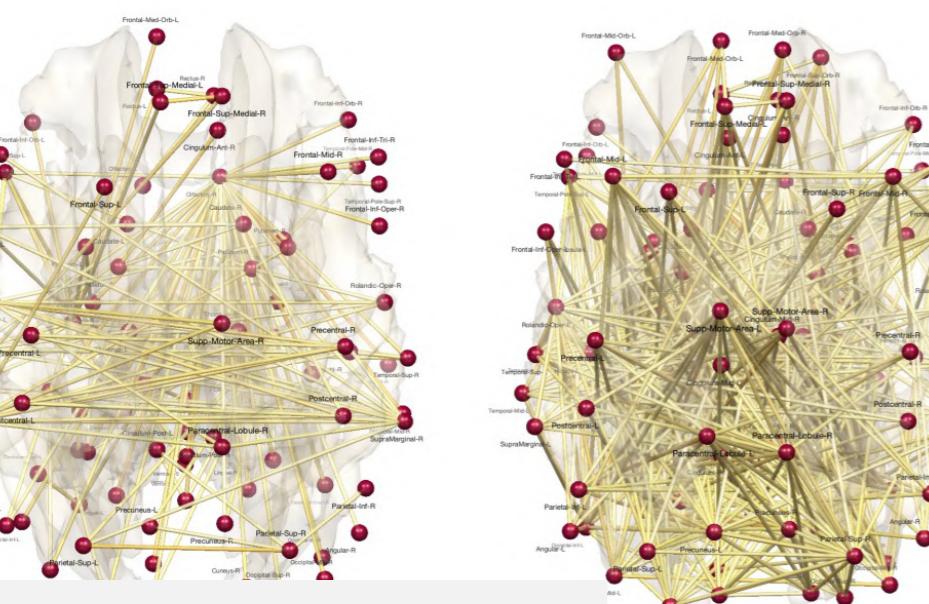


UW-Madison twin study (200 twin pairs)

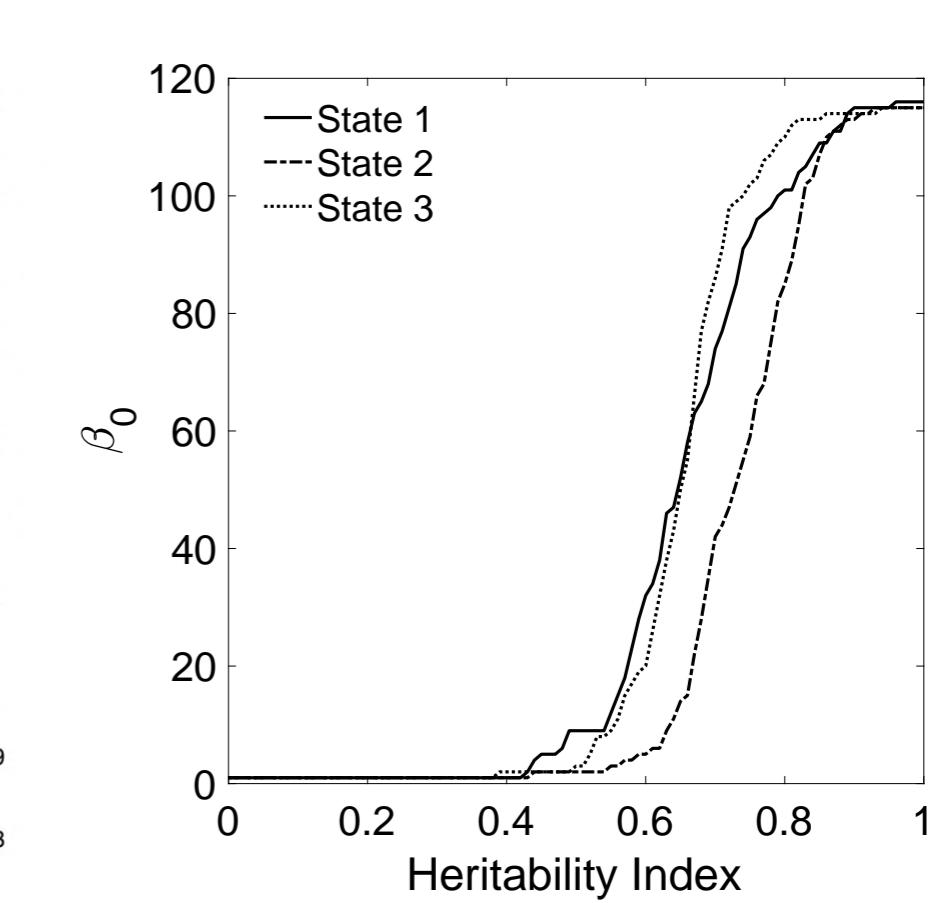
State 1

State 2

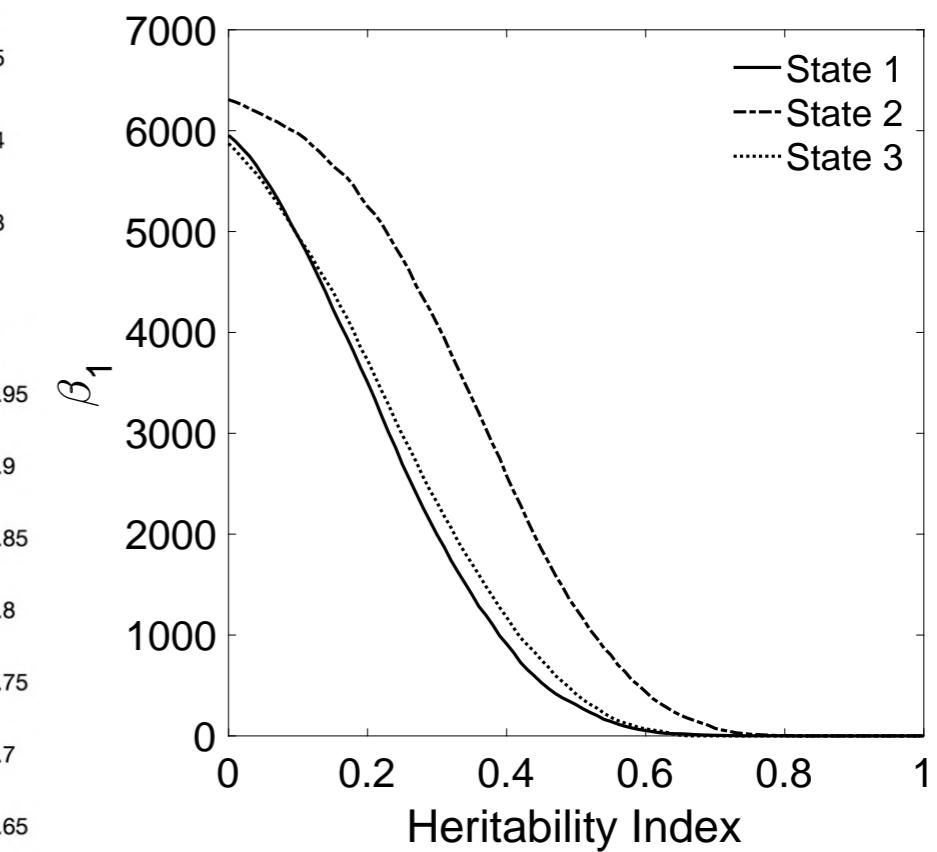
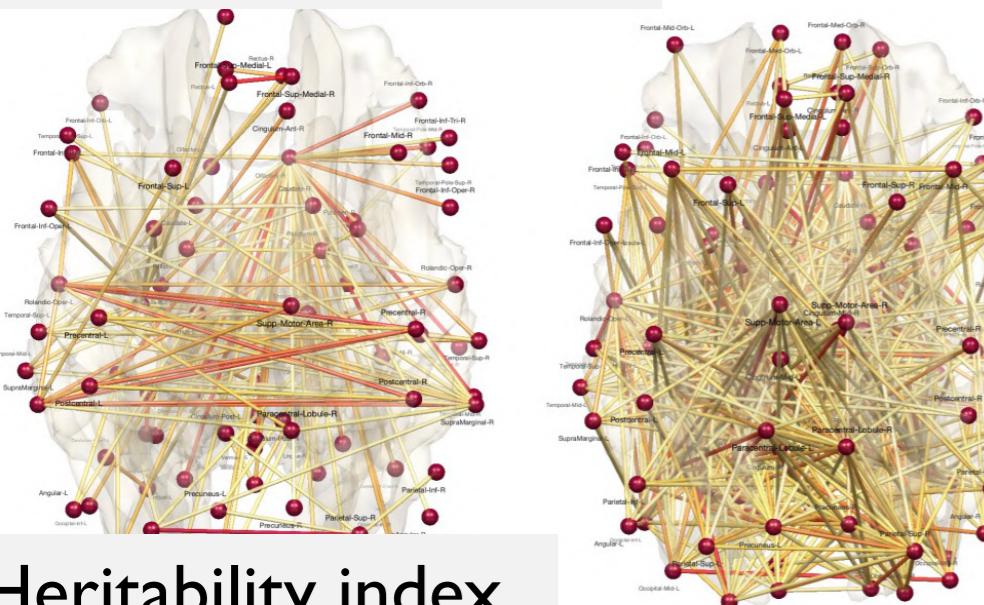
State 3



MZ-twin correlation



DZ-twin correlation



Heritability index

Minisymposium Topological Data Analysis and Machine Learning August 20-25, 2023 Tokyo, Japan



10th International Congress on Industrial and Applied Mathematics

ICIAM 2023 TOKYO

Organizer(s) : Jae-Hun Jung, Shizuo Kaji, Moo K. Chung

Speakers:

- Tomoo Yokoyama (Gifu University)
- Jongbaek Song (KIAS)
- Mason Poter (UCLA)
- Keunsu Kim (POSTECH)
- Peter Bubenik (University of Florida)
- Soham Mukherjee (Purdue University)
- Alexander Strang (Chicago University)
- Mathieu Carriere (INRIA)
- Heather Harrington (Oxford University)
- Jae-Hun Jung (POSTECH)
- Shizuo Kaji (Kyushu University)
- Moo K. Chung (UW-Madison)

Organization for Human Brain Mapping 2024
COEX, June 23-27, 2024, 4000+ attendance

Official satellite meeting
NeuroImaging Statistics Workshop
SNU, Korea June 21-22, 2024, 100+ attendance
Plan to have TDA tutorial for neuroscientists

Organizers :

Moo K. Chung, University of Wisconsin-Madison

Sungkyu Jung, Seoul National University

Tom Nichols, Oxford University

Hernando Ombao, KAUST

Jean-Baptiste Poline, McGill University

Anqi Qiu, National University of Singapore



Thank you.



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postdoc and **graduate research**
if you are better than *chat-GPT*

