University of Wisconsin
SCHOOL OF MEDICINE AND PUBLIC HEALTH

Topological State-Space Estimation of Dynamically Changing Functional Brain Networks

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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(under review in *PLOS Computational Biology*)

Computational Neuroimaging

Neuroscience
+ Mathematics
+ Statistics
+ CS

Magnetic resonance imaging (MRI)

Wisconsin Twin Brain Imaging Study done here

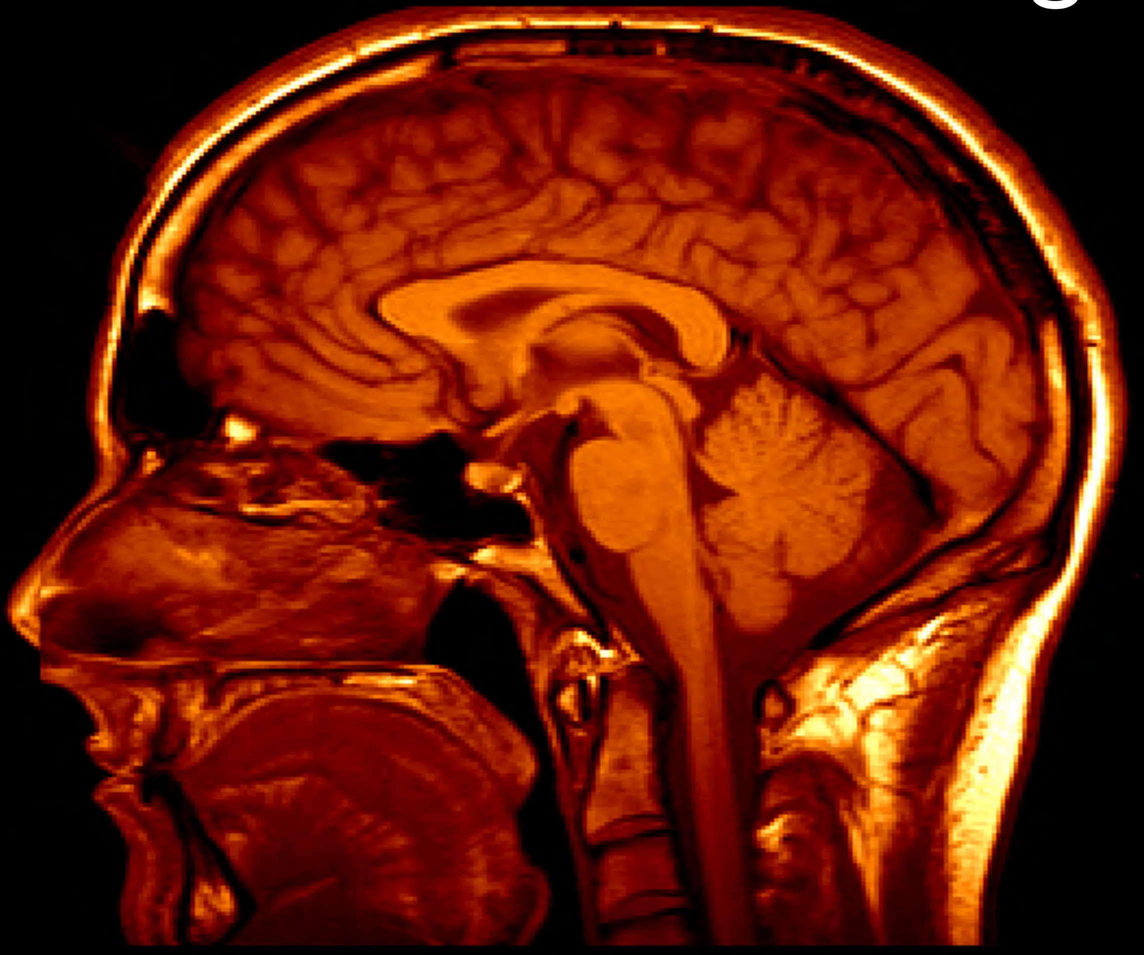
3T GE Discovery X750
Waisman Brain Imaging Laboratory
University of Wisconsin-Madison

Magnetic Resonance Imaging (MRI)

3.0 Tesla GE Scanner

Soft tissues

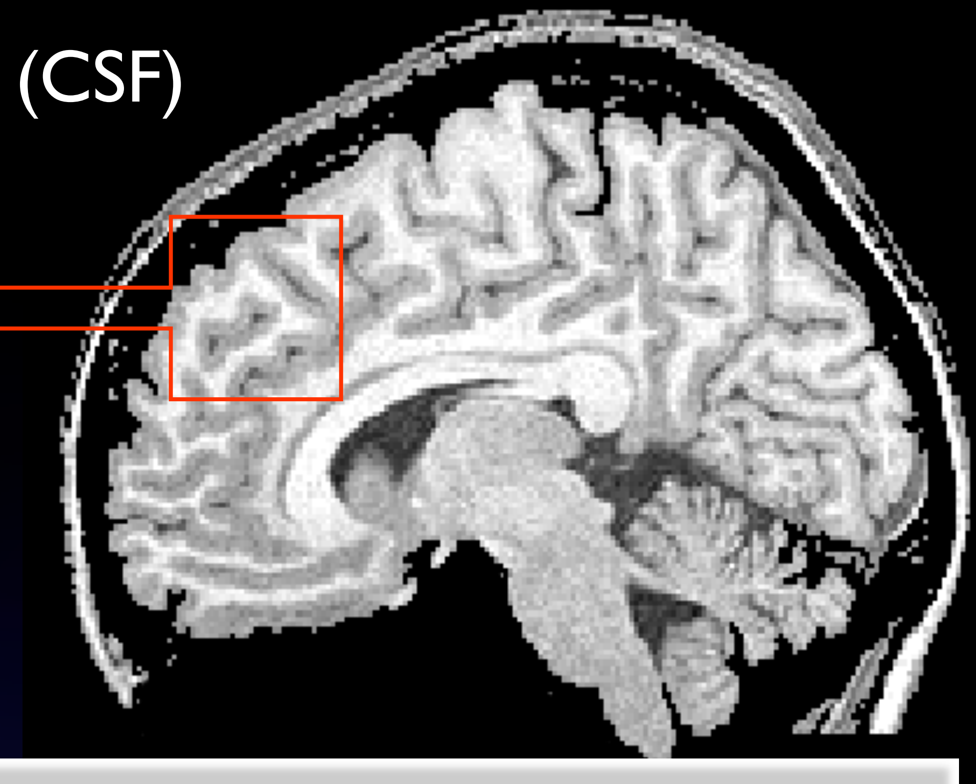
3D image



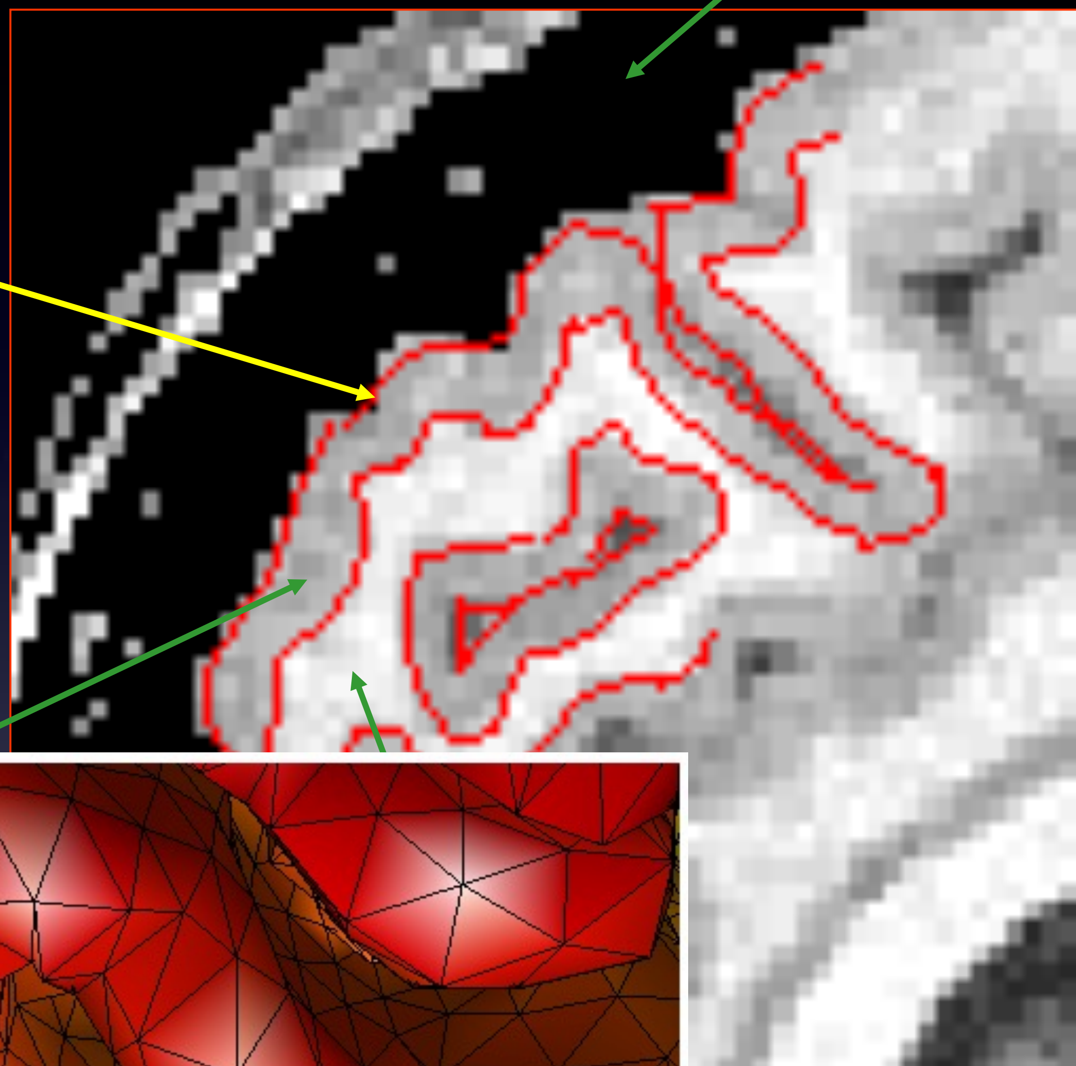
Soft tissues: brain

Basic brain anatomy

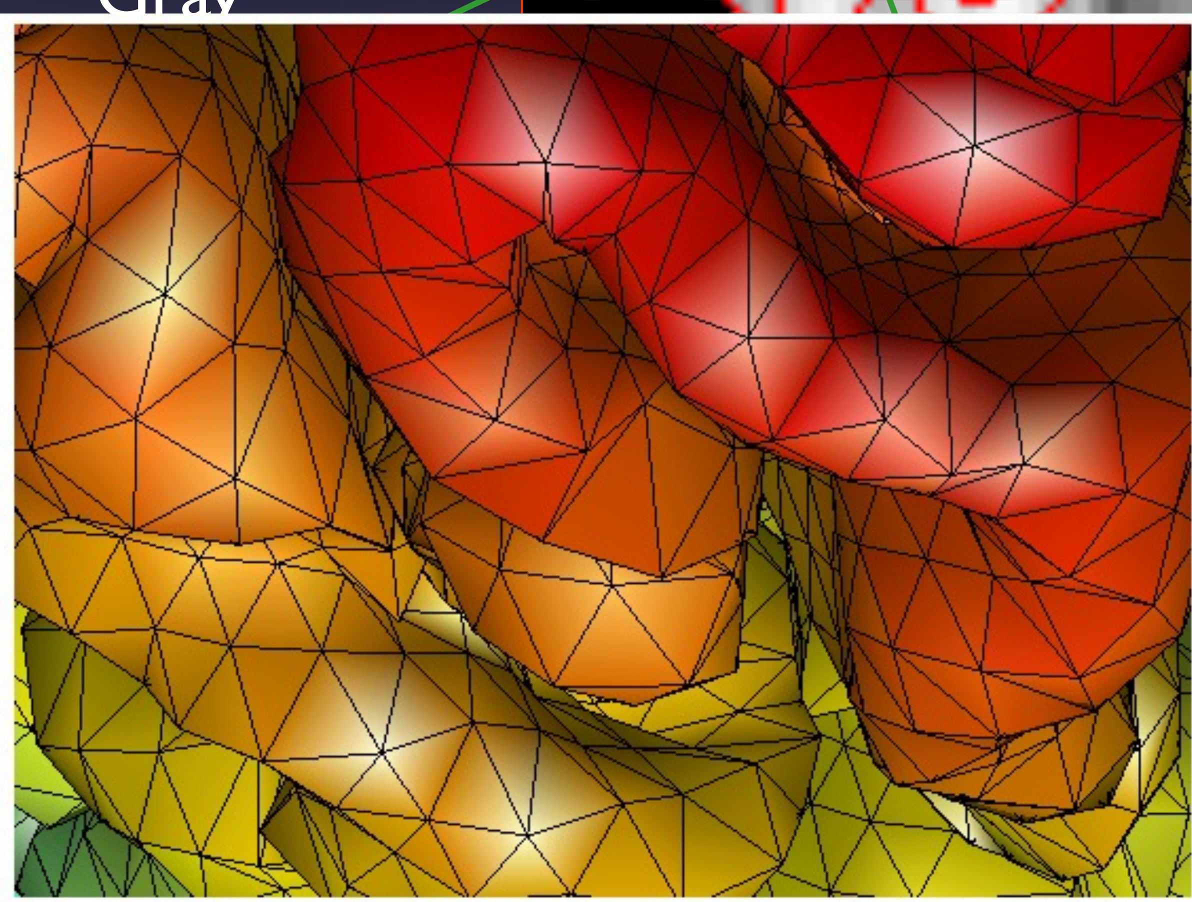
Cerebral Spinal Fluid (CSF)

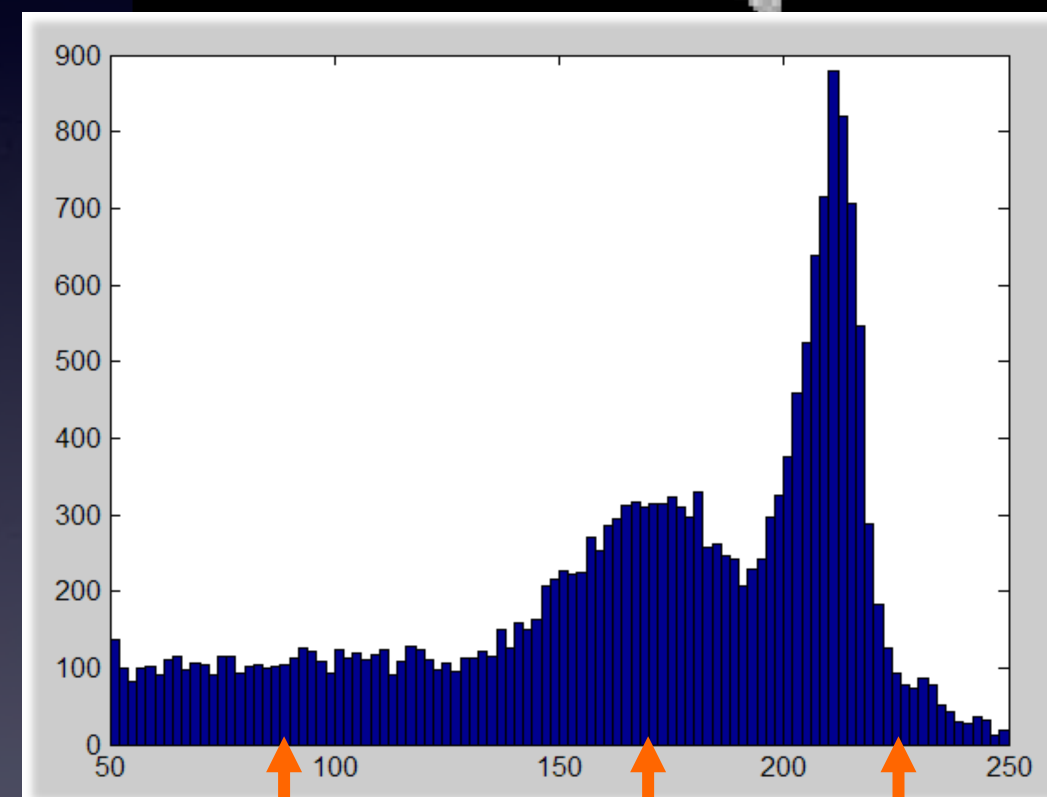


Outer Cortical Surface



Gray

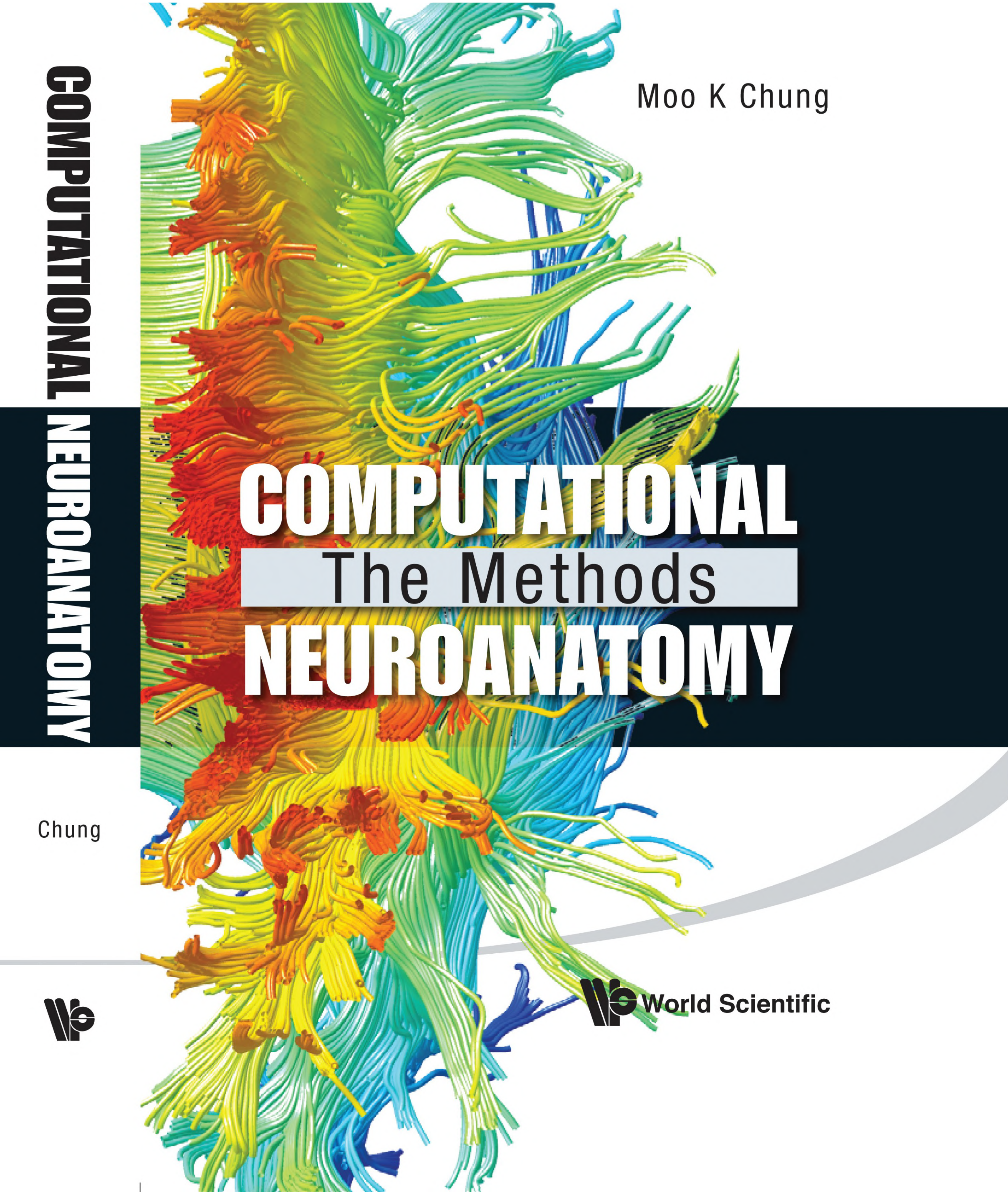




CSF Gray White

3 component Gaussian mixture

computational neuroanatomy



Mathematics
Computer Science
Statistics
Neuroimaging

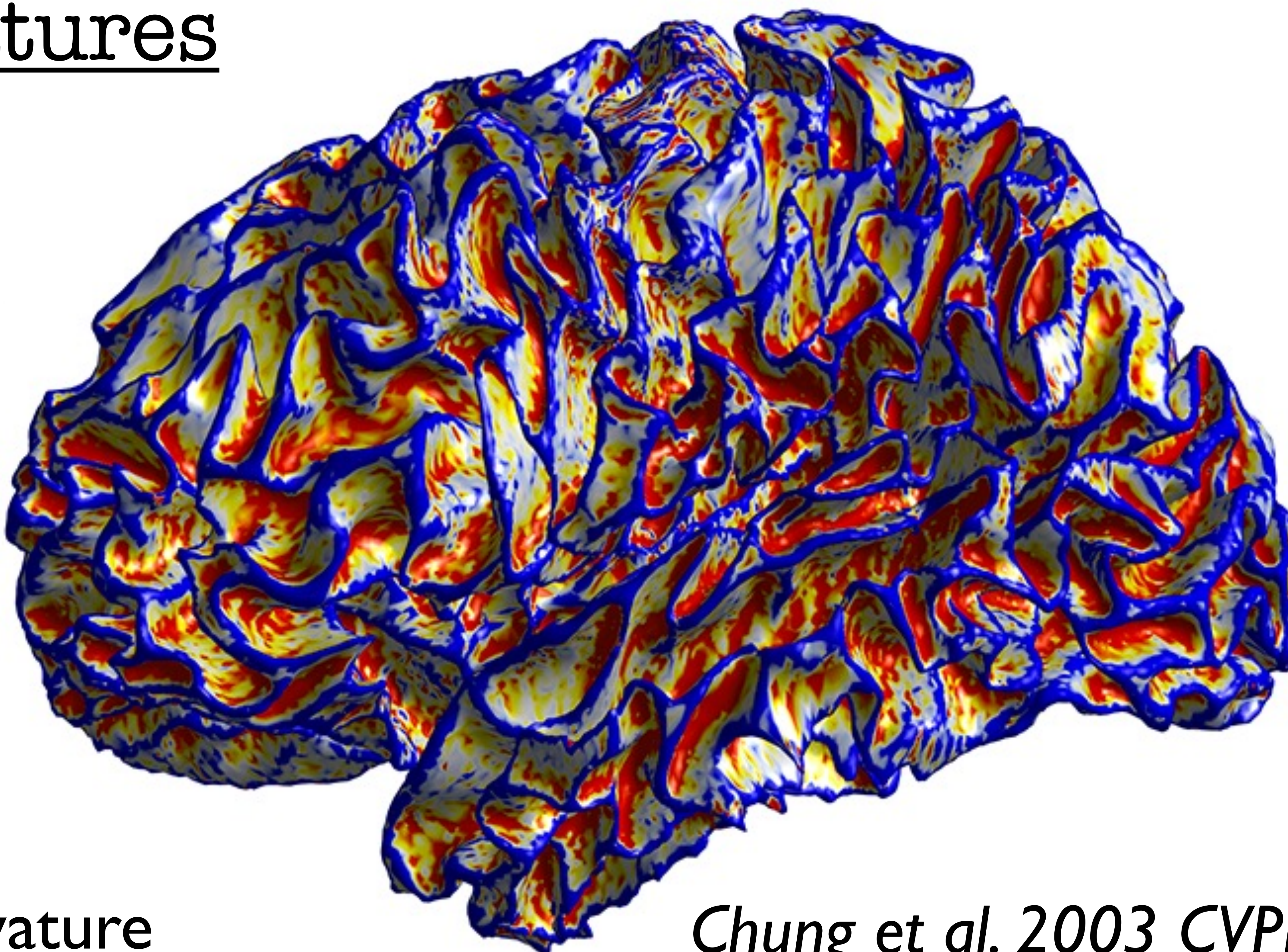
↓

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

Code and sample data

https://github.com/laplcebeltrami/curvatures

MATLAB



Mean curvature

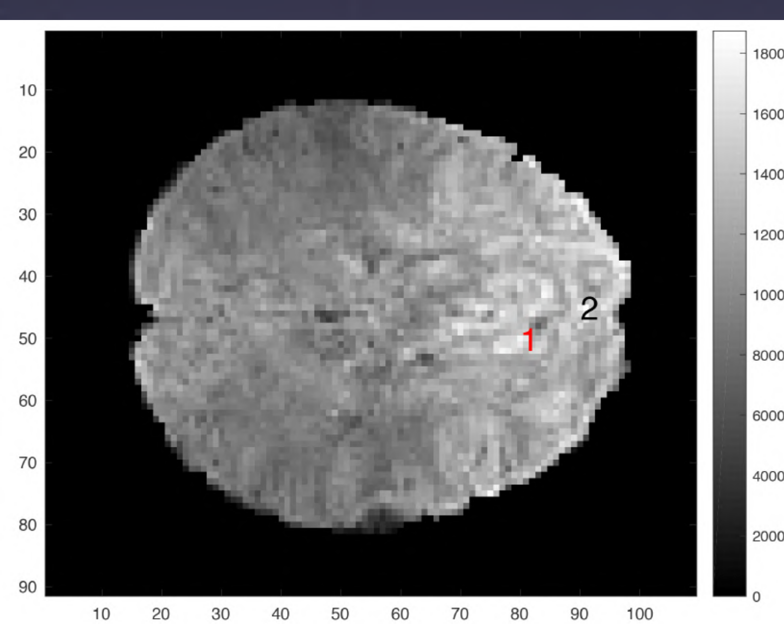
Chung et al. 2003 CVPR

Functional Magnetic Resonance Imaging (fMRI)

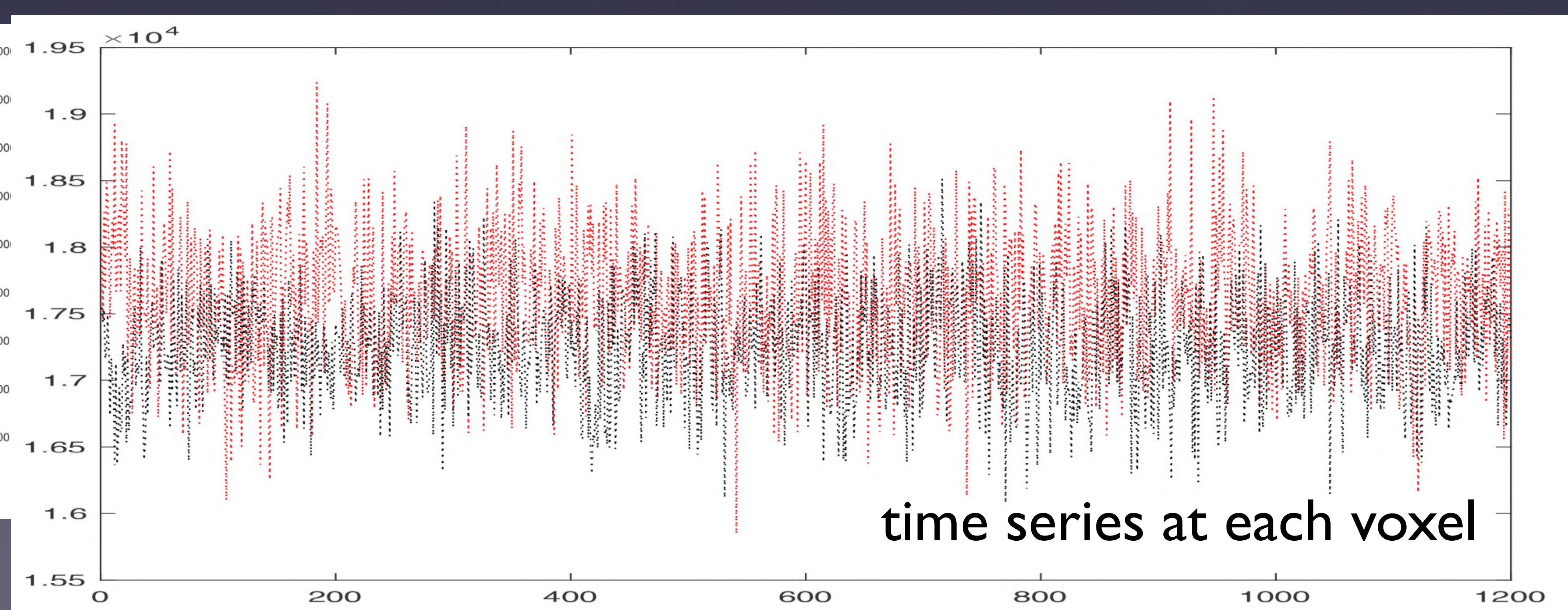
3.0 Tesla GE Scanner

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

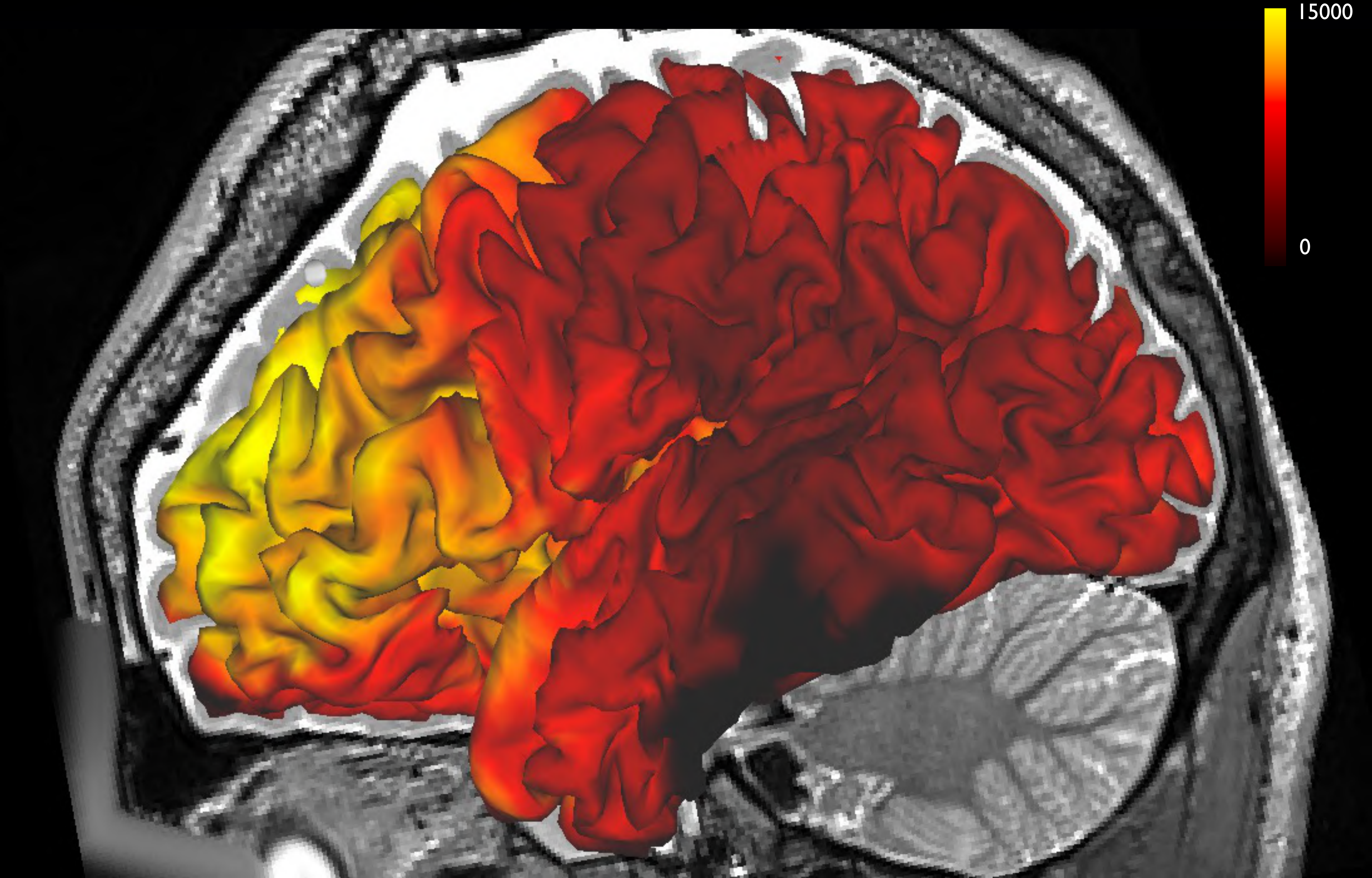
416 subjects (131 MZ twins 77 DZ twins) x 2GB = 832GB data



Blood oxygenation level



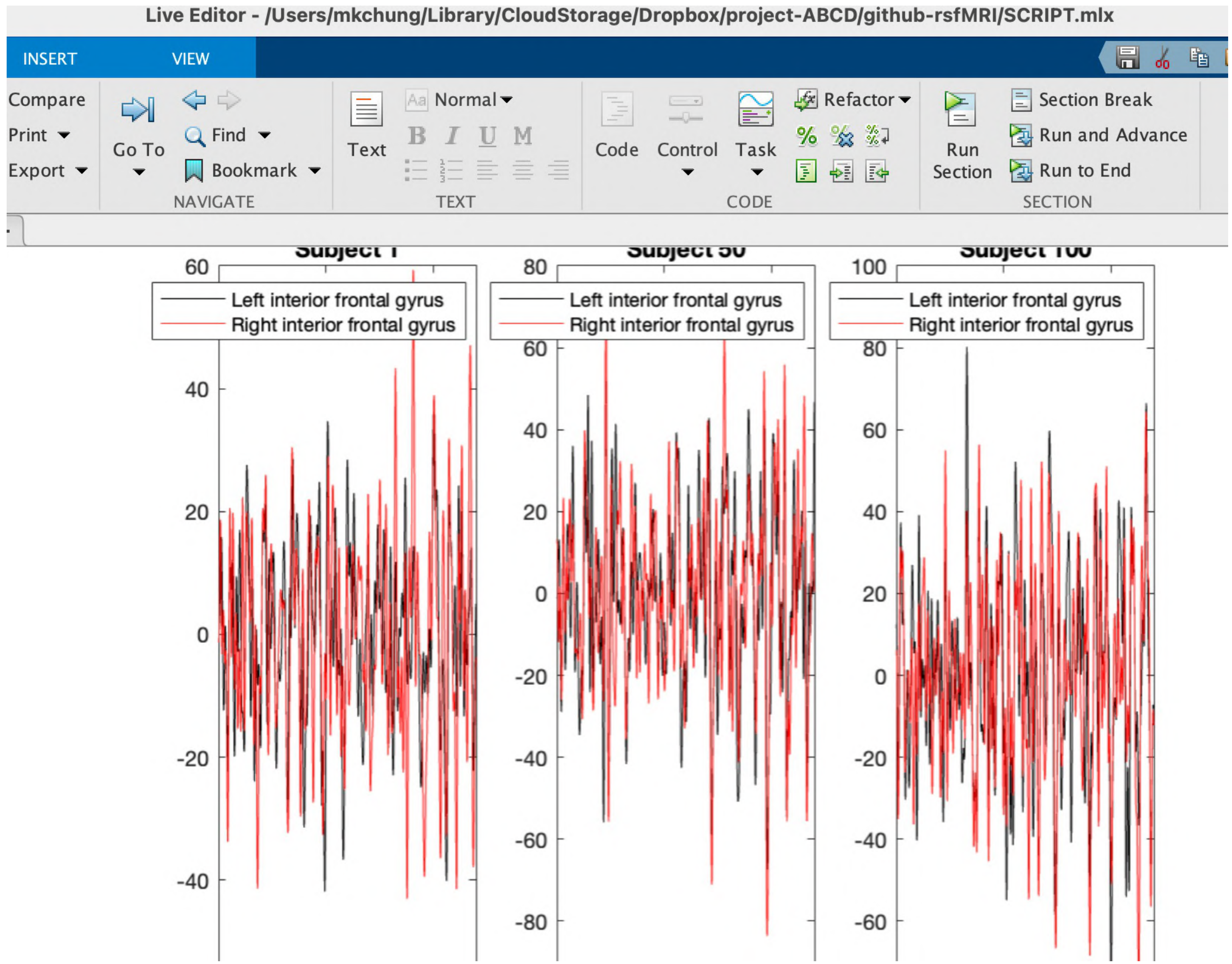
Typical rs-fMRI (every 30 second)



Code and sample data

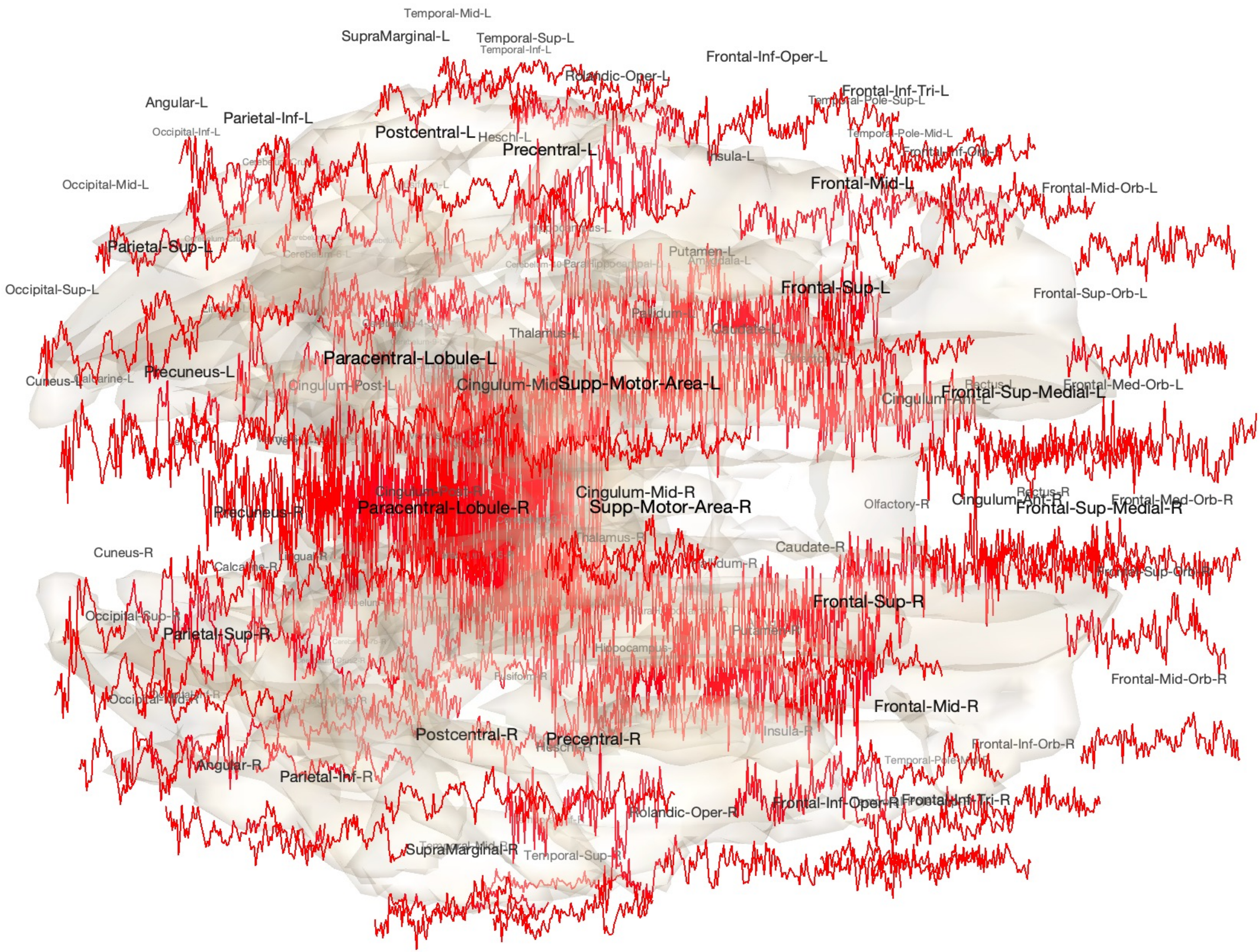
https://github.com/laplcebeltrami/rsfMRI

MATLAB

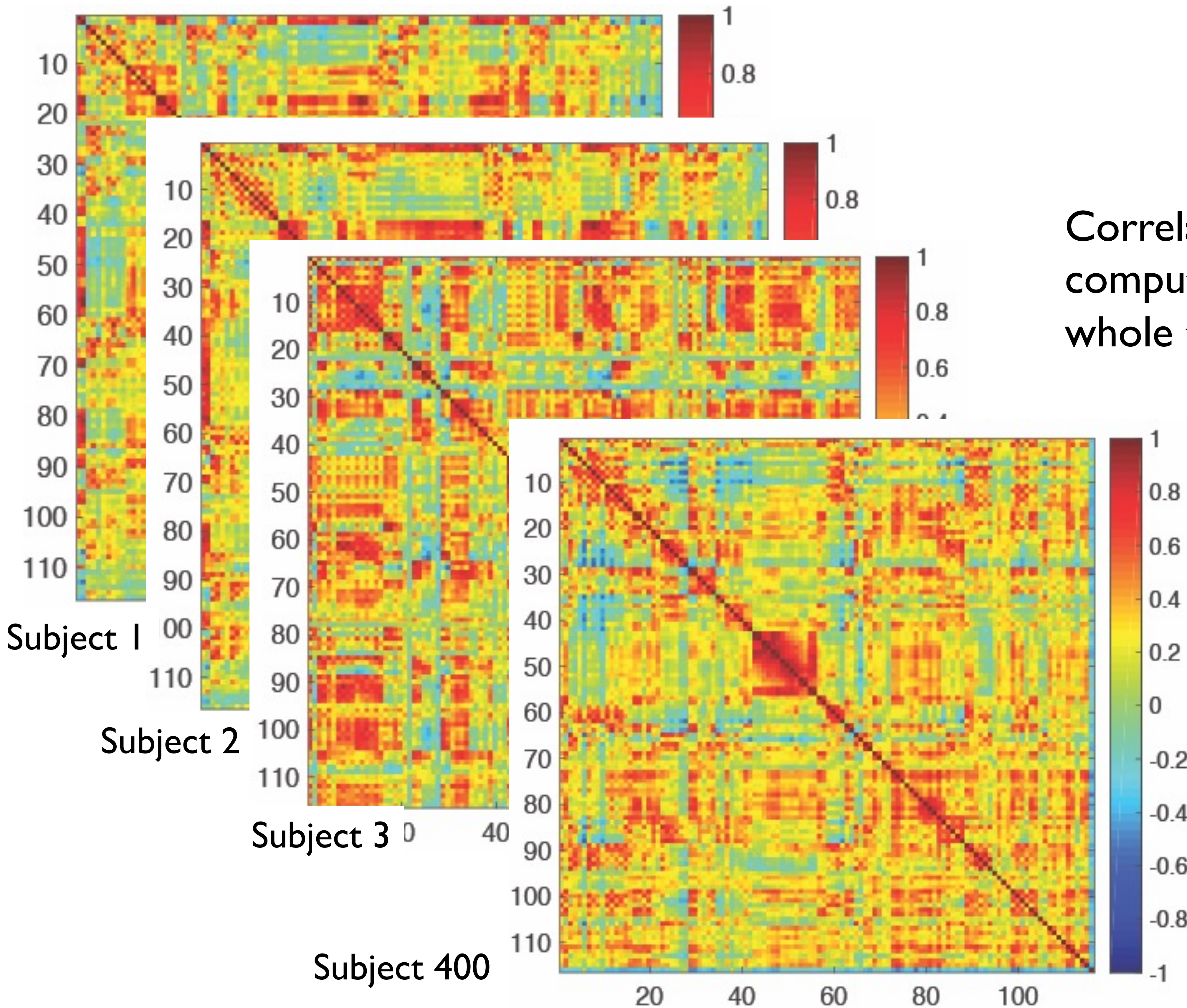


Huang et al. 2020 Neuroscience Methods

Time series averaged into 116 brain regions

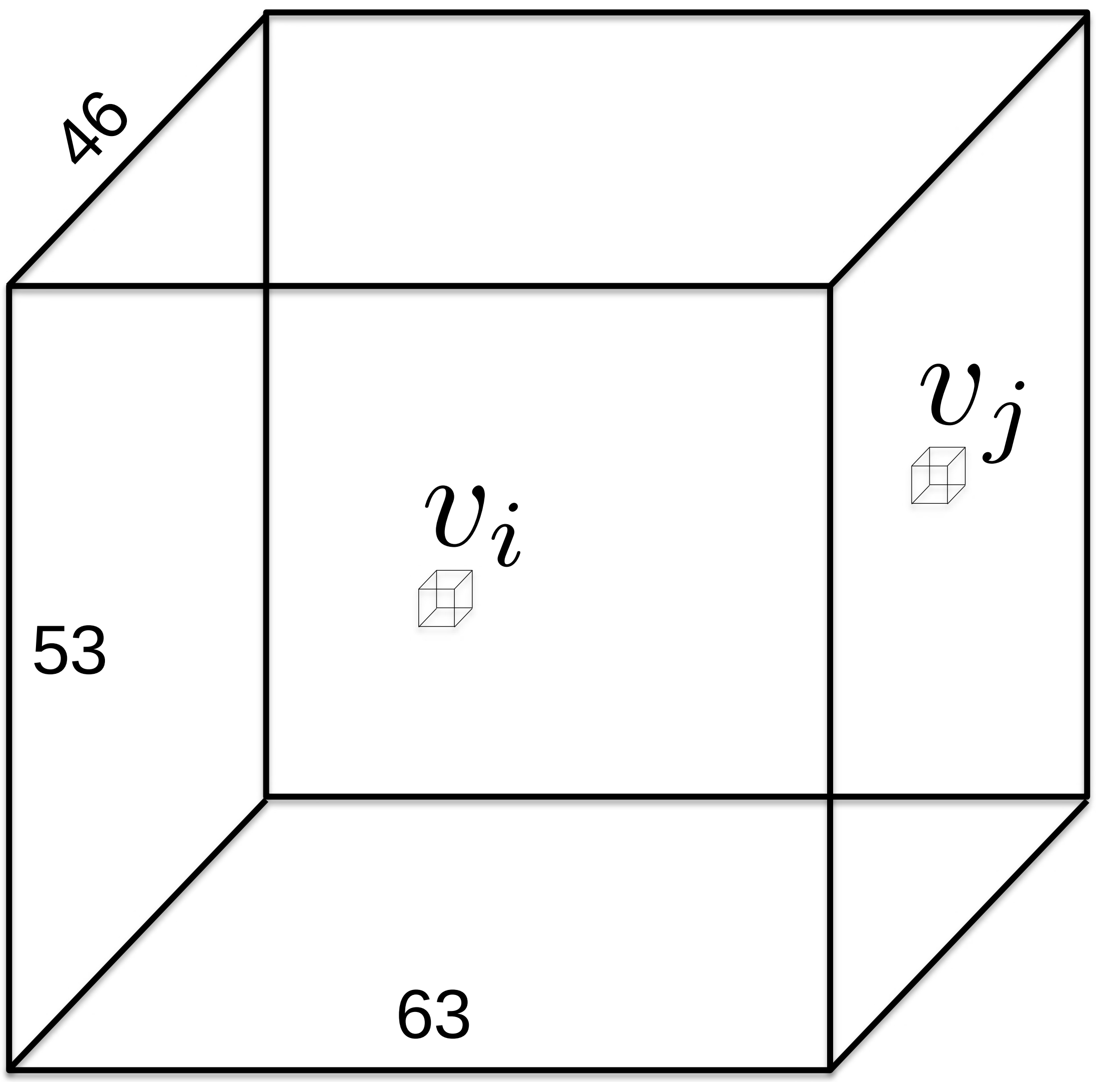


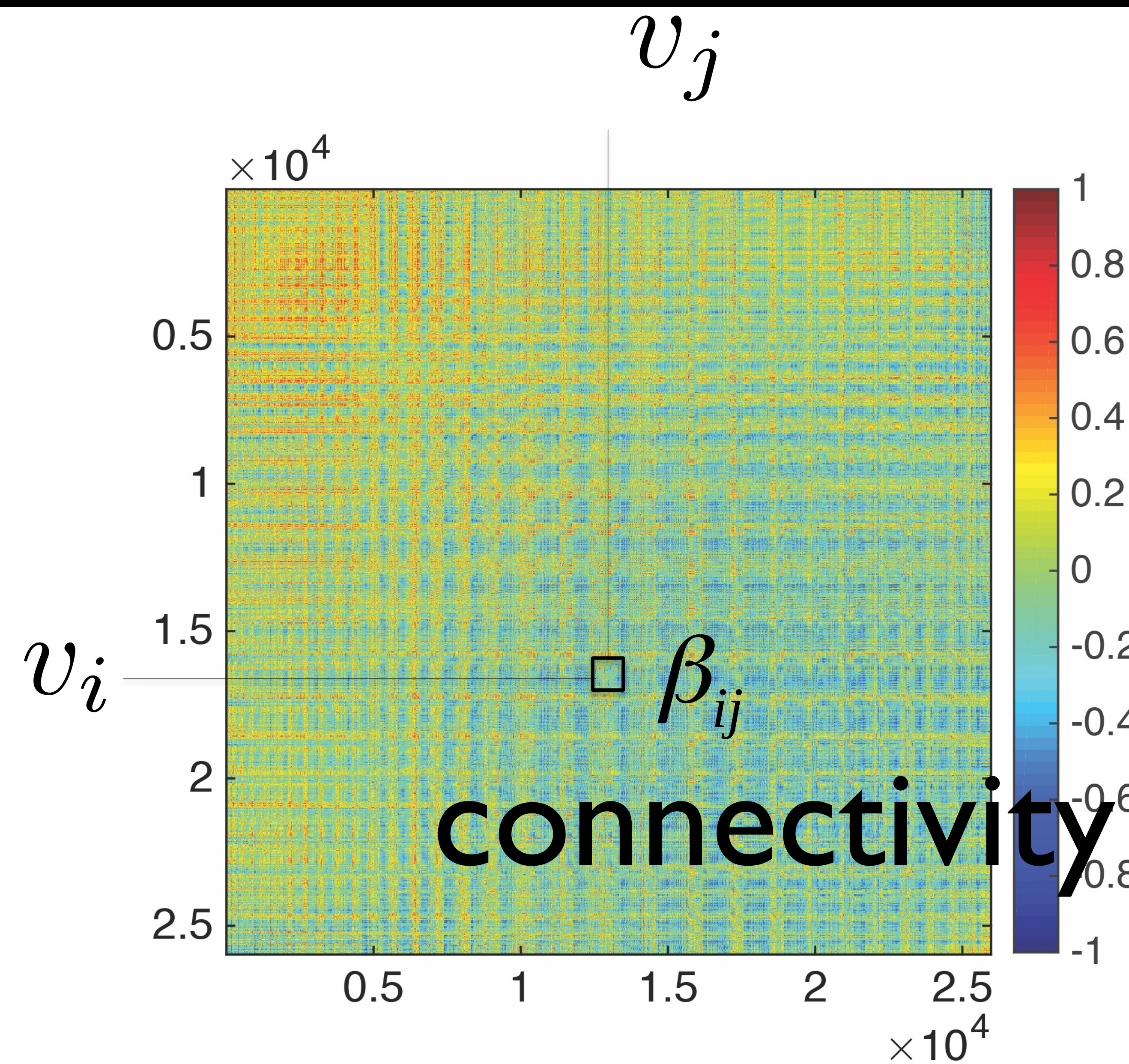
Subject level brain connectivity matrix



Correlation computed over whole time points

How big is fMRI connectivity data?



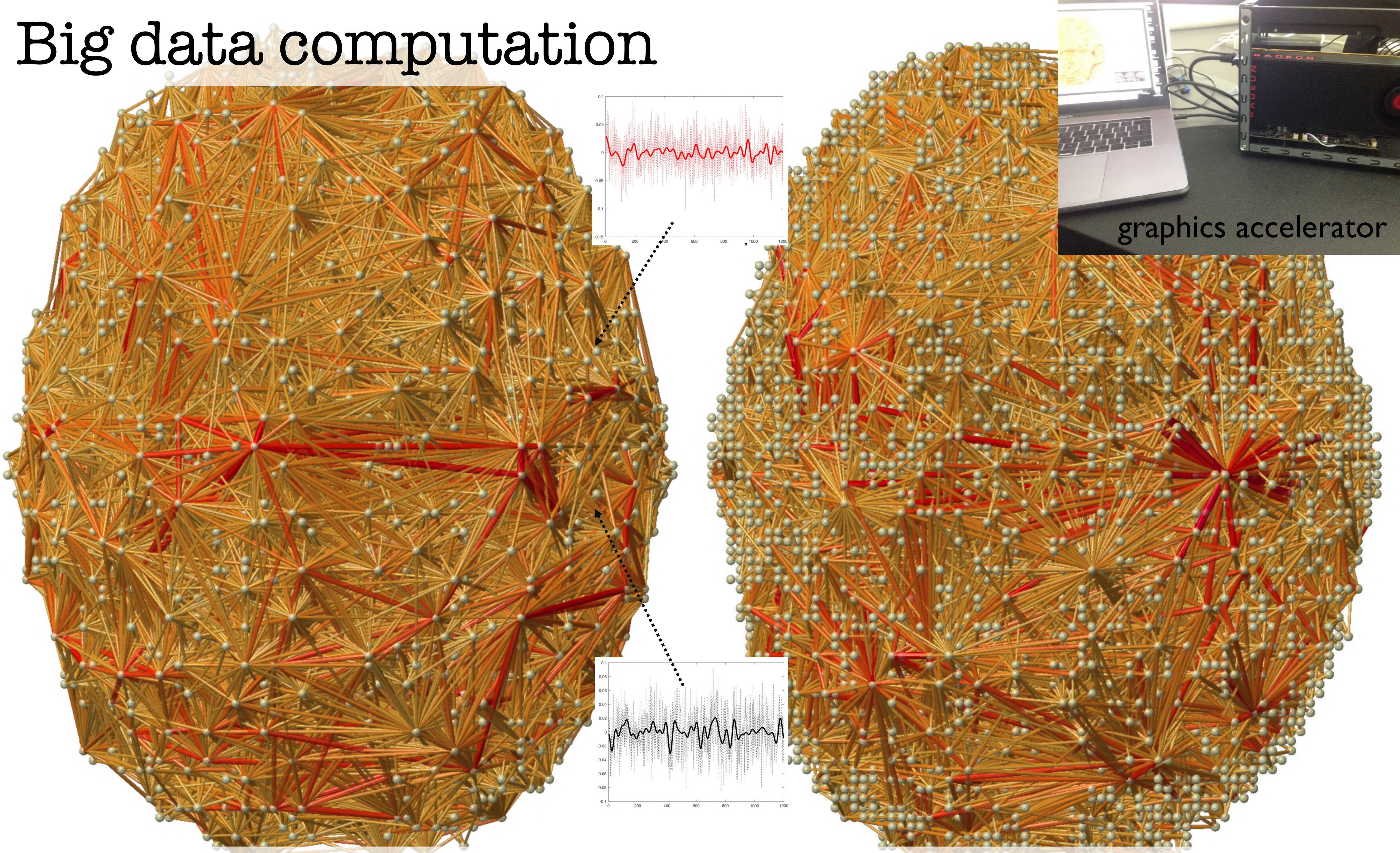


p=25972 voxels (1.5T at 3mm resolution) in the brain

25972 x 25972 = 0.67 billion connections

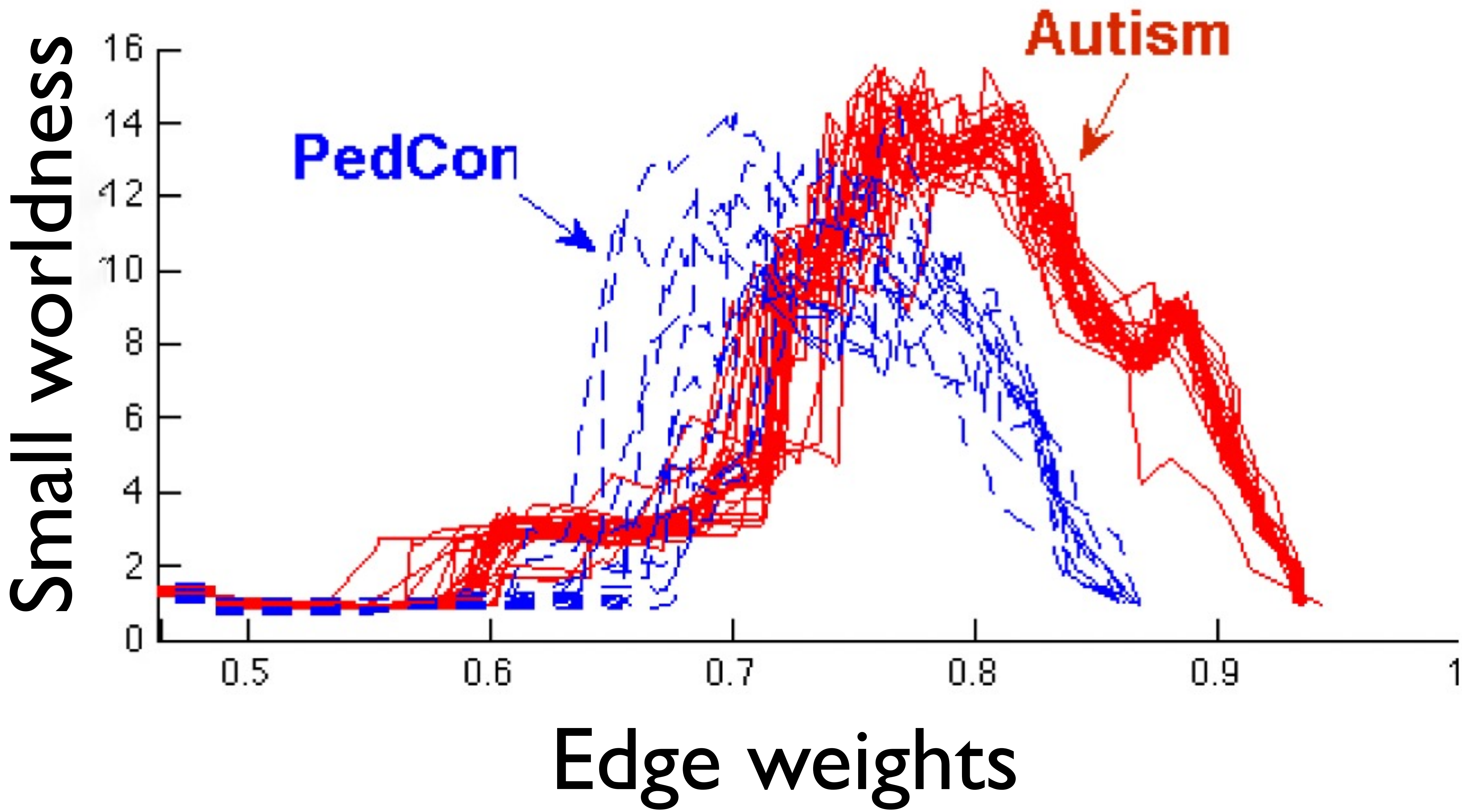
5.2GB data

Big data computation

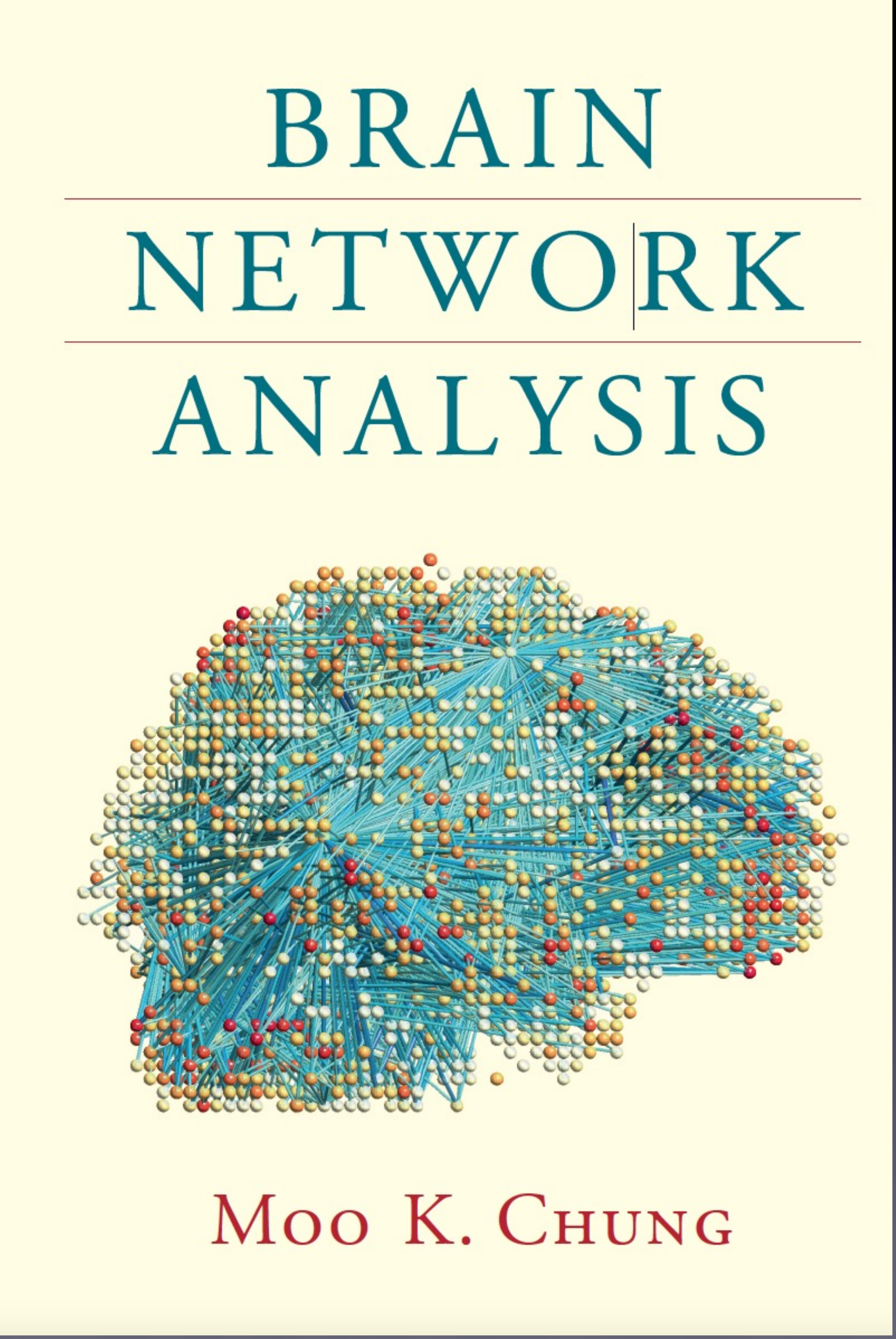


Resting state brain network obtained from functional-MRI.
Correlation of 300000 time series in the brain.
For 3D rendering, subsampled at 25000 nodes.

Graph theory features → Often incorrect conclusion



Lee et al. 2011 IEEE Transactions on Medical Imaging 30:1154-1165

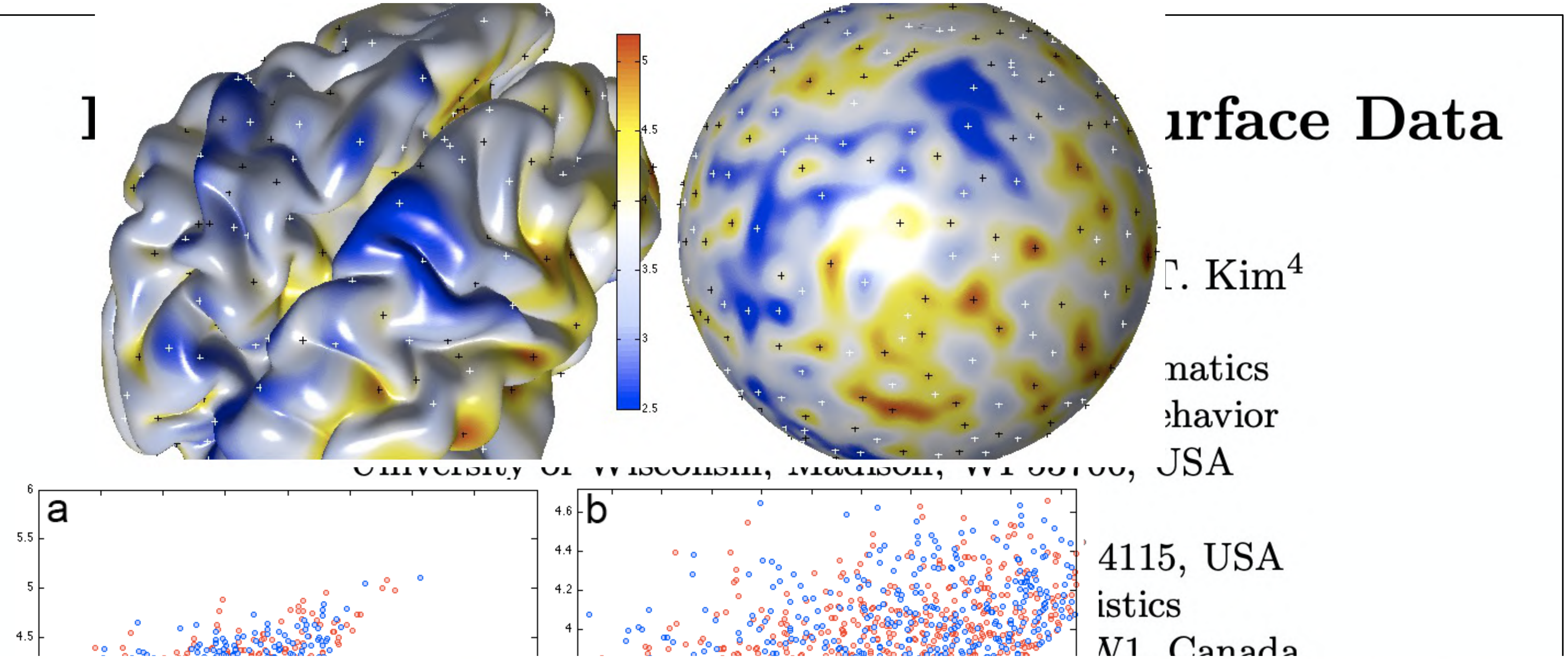


Book writing with Cambridge University Press on tutorial style applied-TDA

Chung, 2019
Cambridge University Press

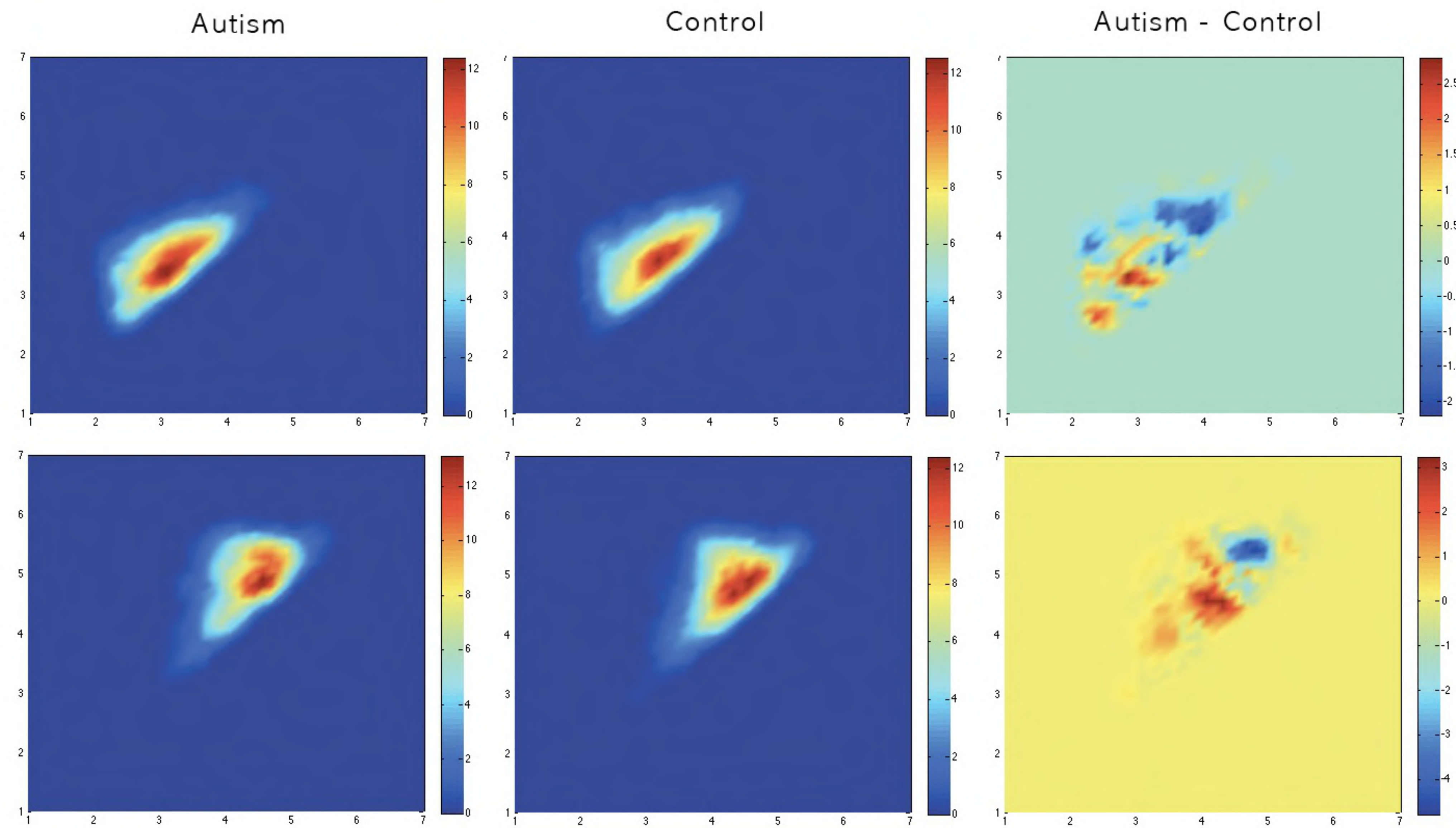
Topological data analysis (TDA)

Completely data driven!
No model!
No distributional assumption!



<ins>*Chung et al., 2009*</ins>

Information Processing in Medical Imaging (IPMI) 5636:386-397.



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

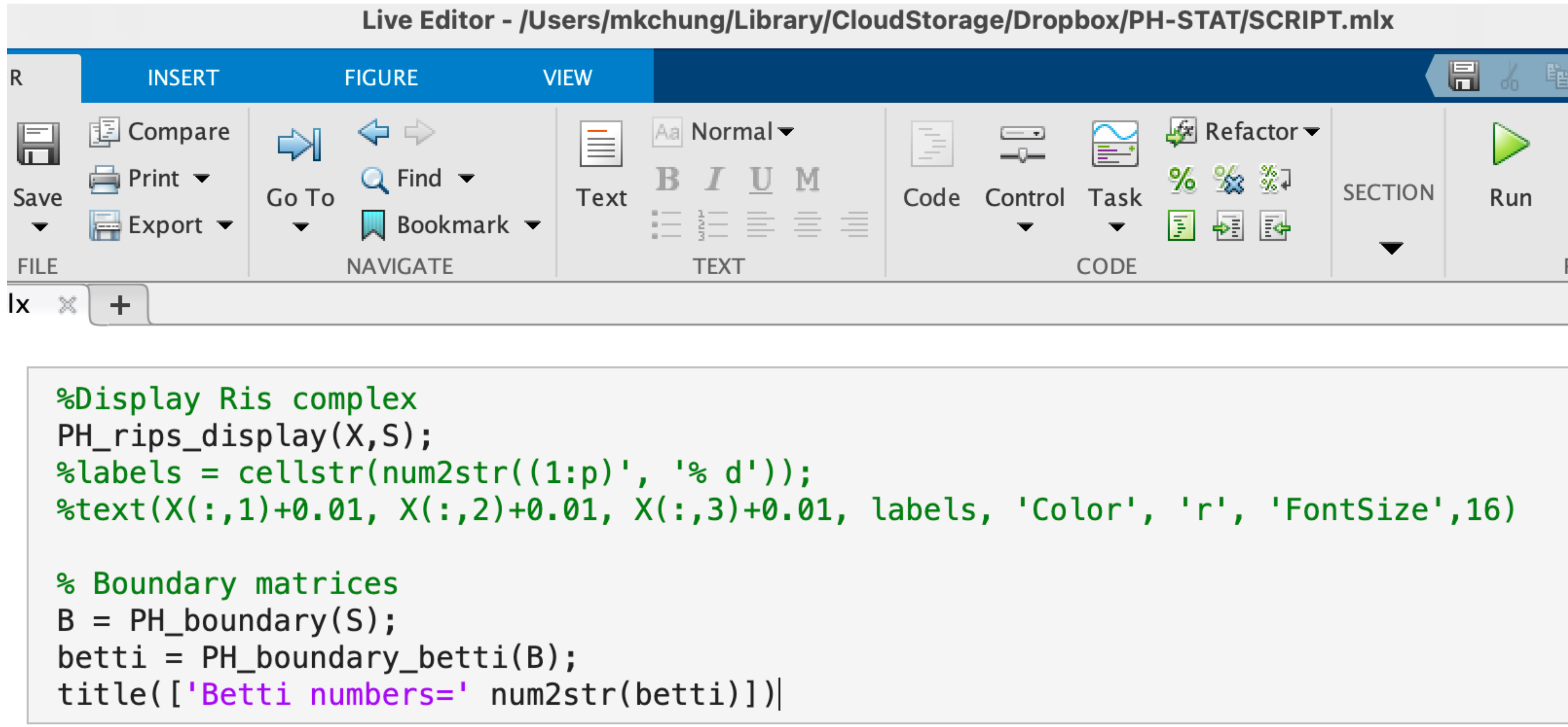
Manual:

Chung (and CHAT-GPT) 2023, PH-STAT arXIv:2304.05912

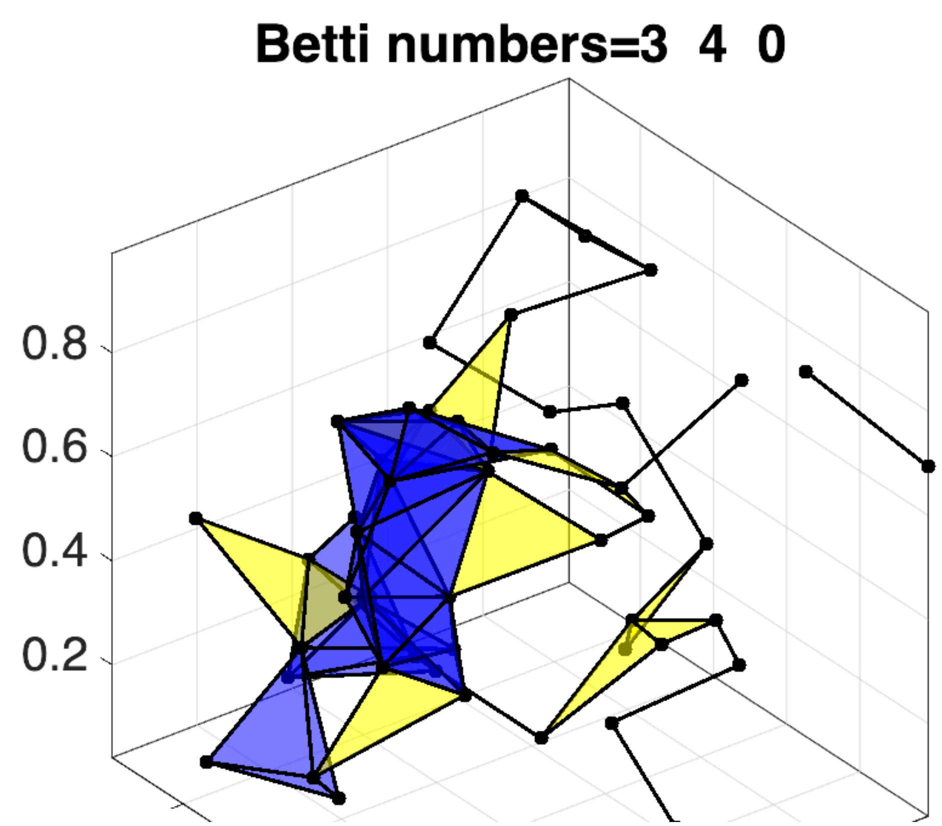
The codes are used to publish topological data analysis papers in leading journals and conferences since 2009:

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



Planning for NIH tool development grant



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
```

```
S =
  4×1 cell array
    { 50×1 double}
    {101×2 double}
    { 73×3 double}
    { 27×4 double}

S{1} =      %Nodes indexing
     1
     2
     3
     4
     ...
```

```
S{2}=   %Edge indexing
   1   5
   1   9
   1  13
   ...

S{3}= %Face indexing
   1   5  13
   1   5  16
   1   5  26
   ...
```

```
S{2}(1,:)=
   1   5
```

```
%Lexicographical indexing
```

Open problem:

Build functions on top of simplicial complexes

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

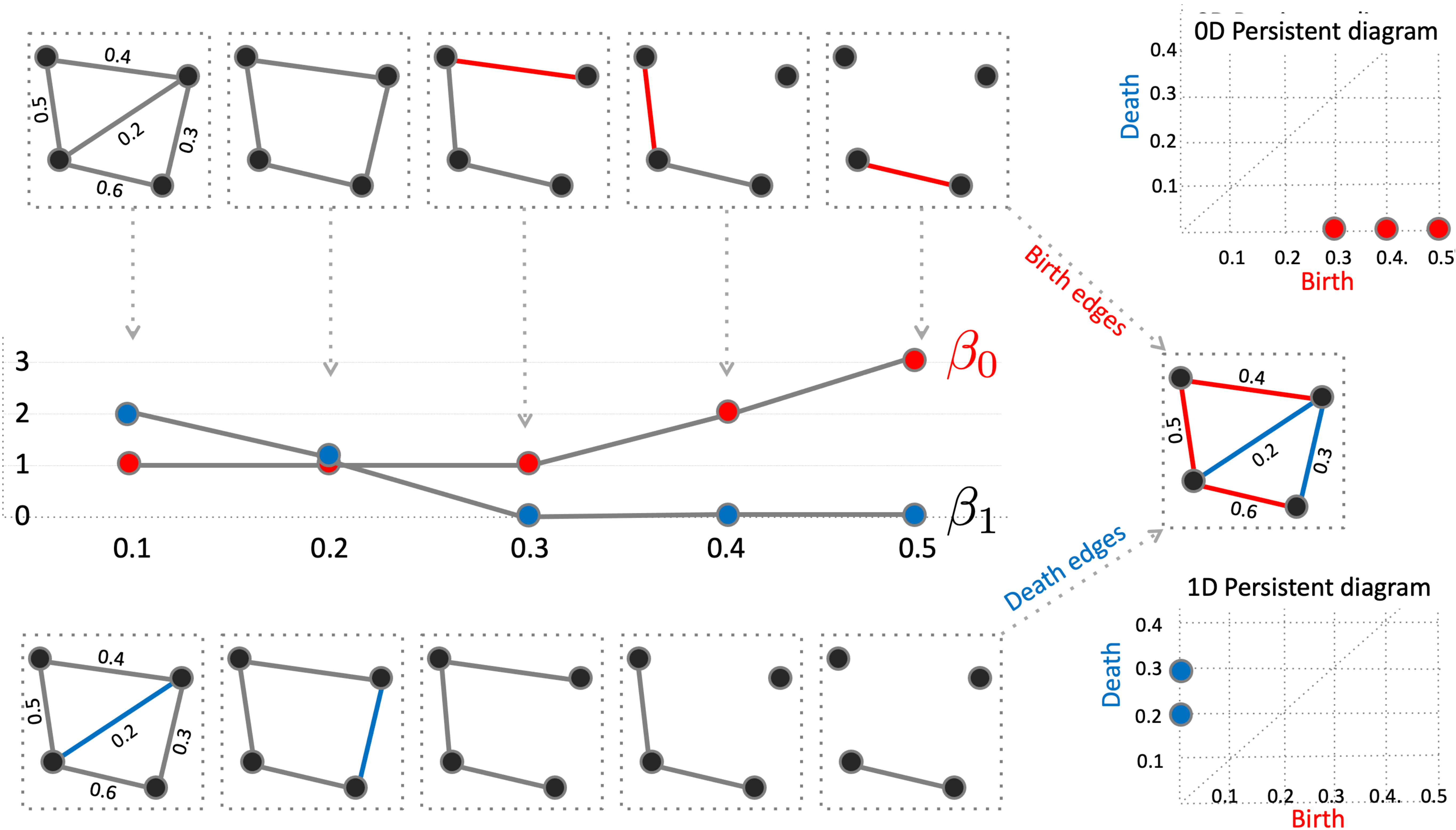
$$\epsilon_0 < \epsilon_1 < \epsilon_2 < \cdots$$

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

Lee et al. 2011 MICCAI 6892:302-309

Chung et al. 2019 Network Neuroscience 3:674-694

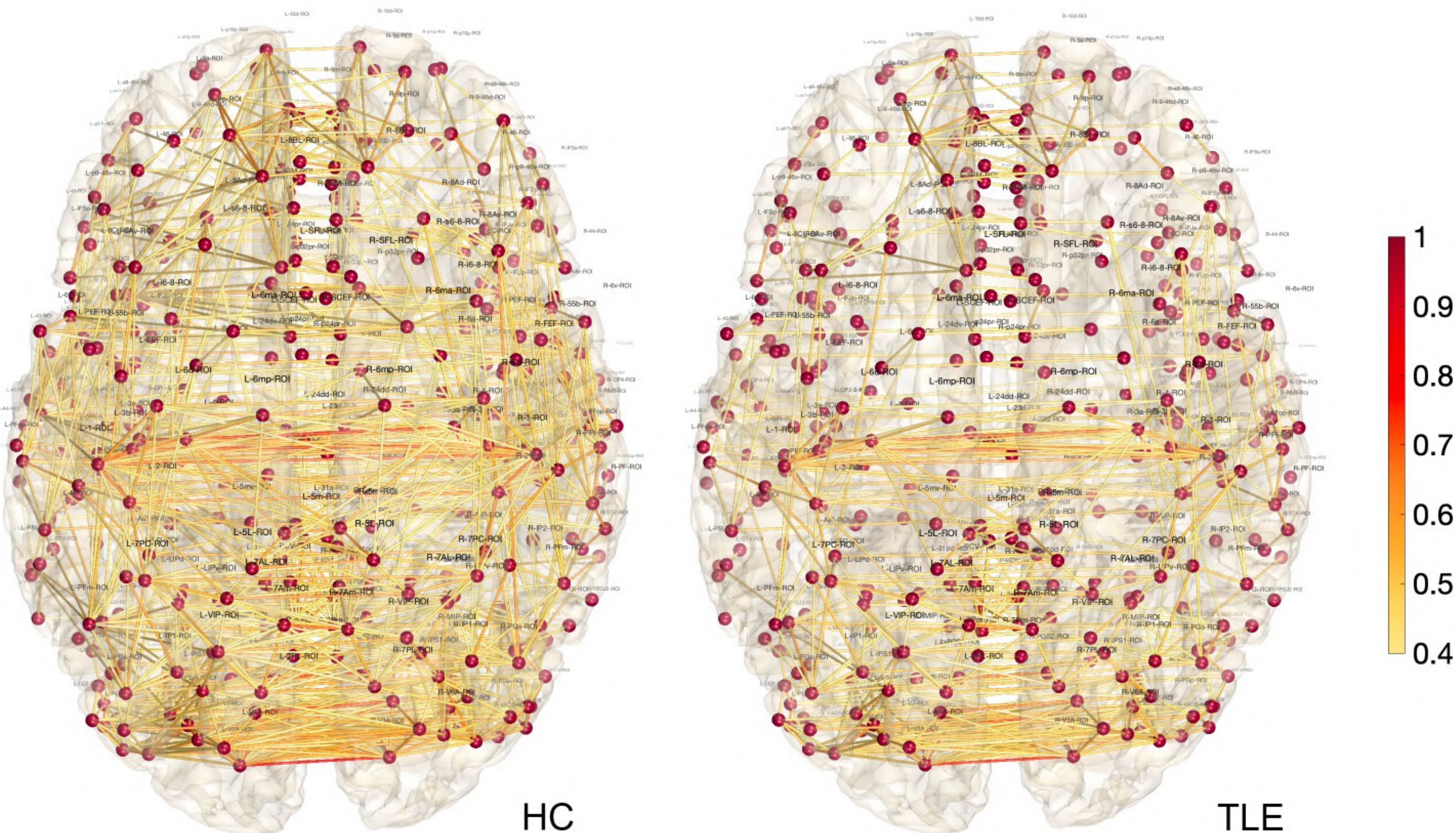
Theorem: Birth & death decomposition



Songdechakraiwut and Chung. 2023, Annals of Appled Statistics 17:403-433

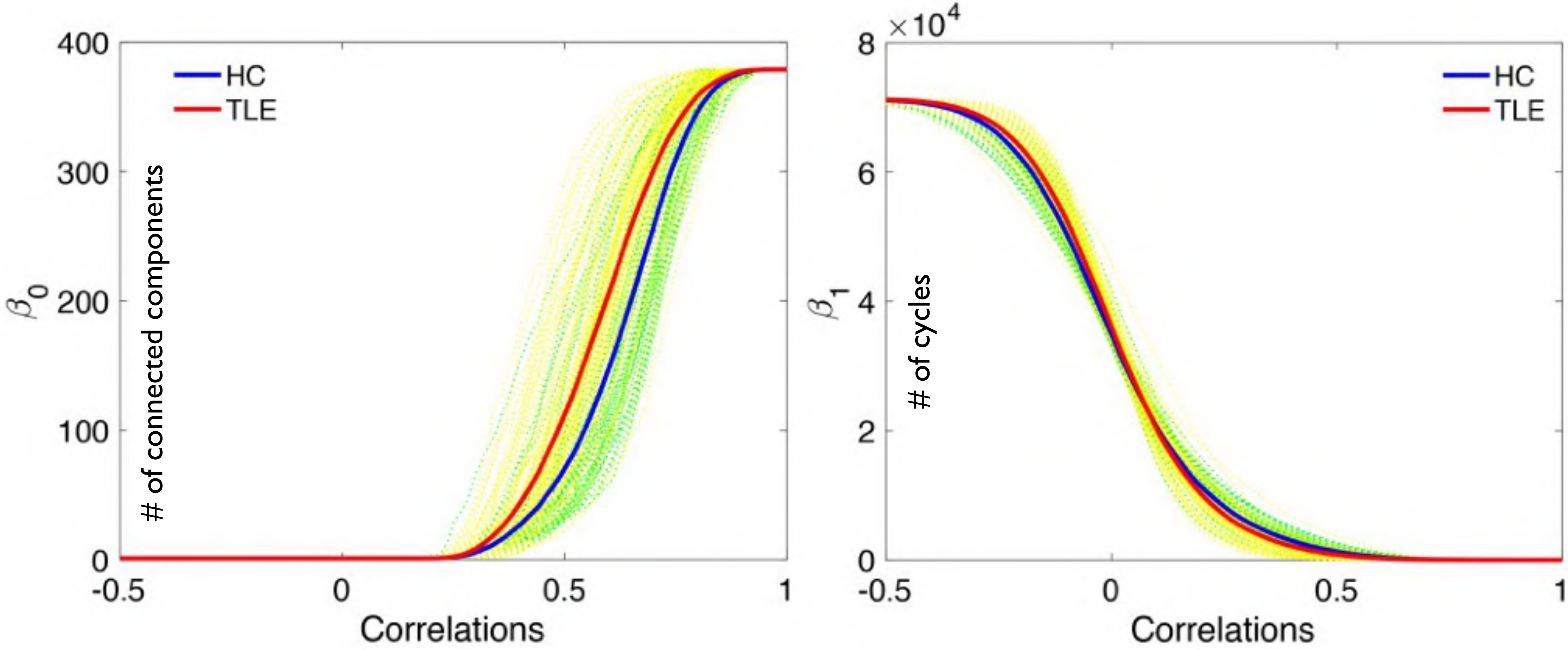
Average correlation networks

50 healthy controls   101 temporal lobe epilepsy



How much they differ topologically?

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



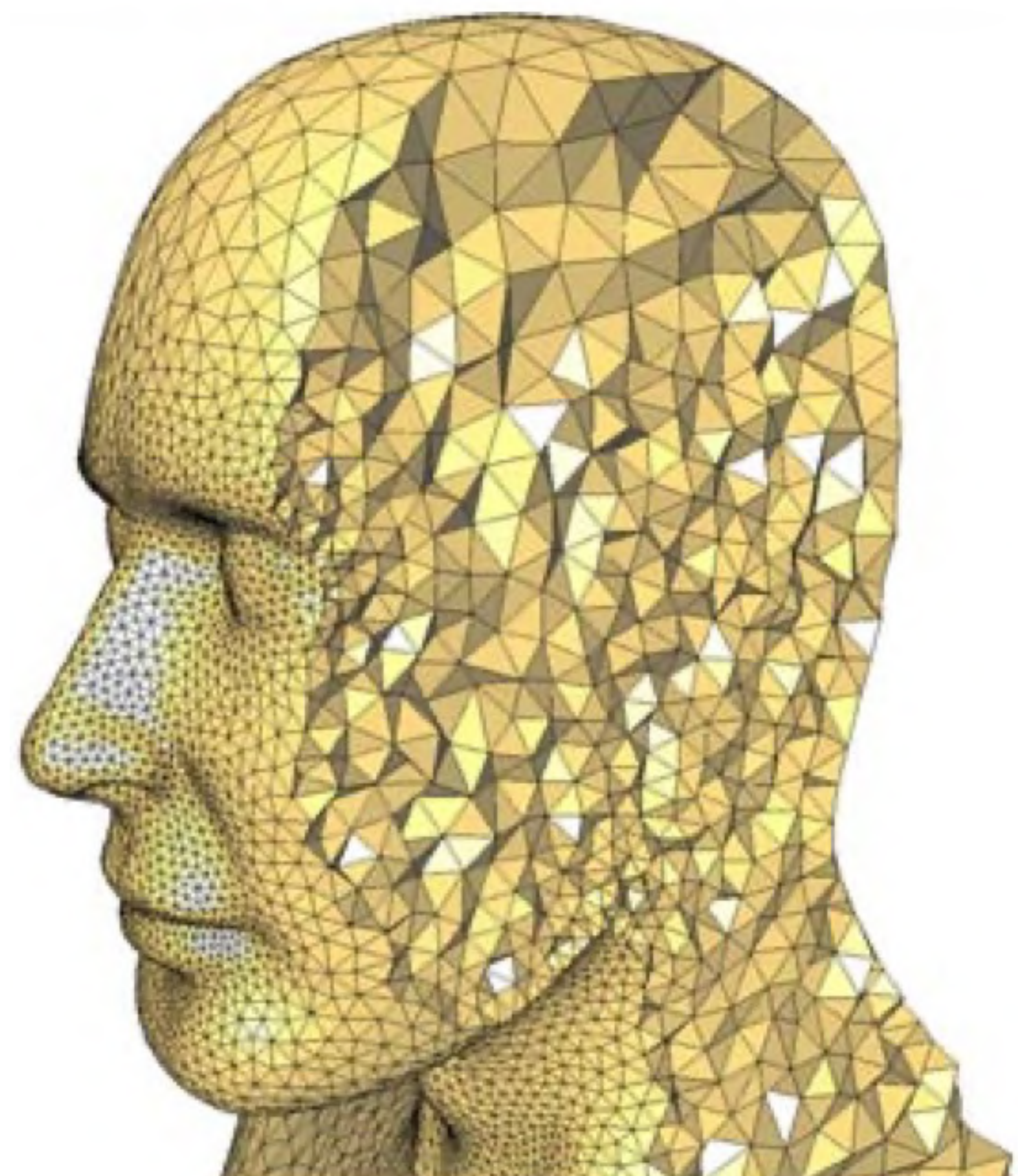
TLE has more disjoint subnetworks.

Open research problem

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

$\beta_2, \beta_3, \cdots$ are monotone?

Example: Tetrahedral mesh

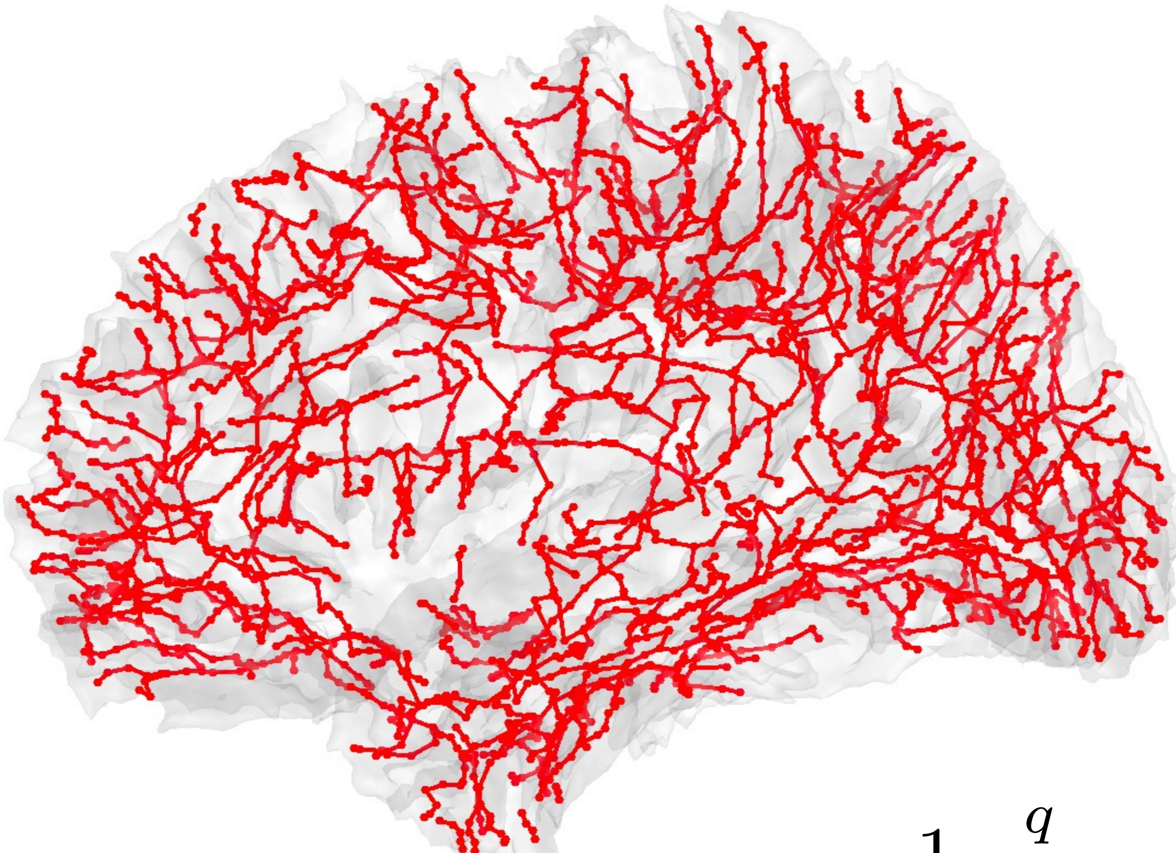


Alliez et al. 2005 ACM SIGGRAPH

2-Wasserstein distance between scatter points

Random variables: $X \sim f_1 \quad Y \sim f_2$

2-Wasserstein distance: $\mathcal{D}(X,Y) = \big(\inf \mathbb{E}\|X - Y\|^2\big)^{1/2}$



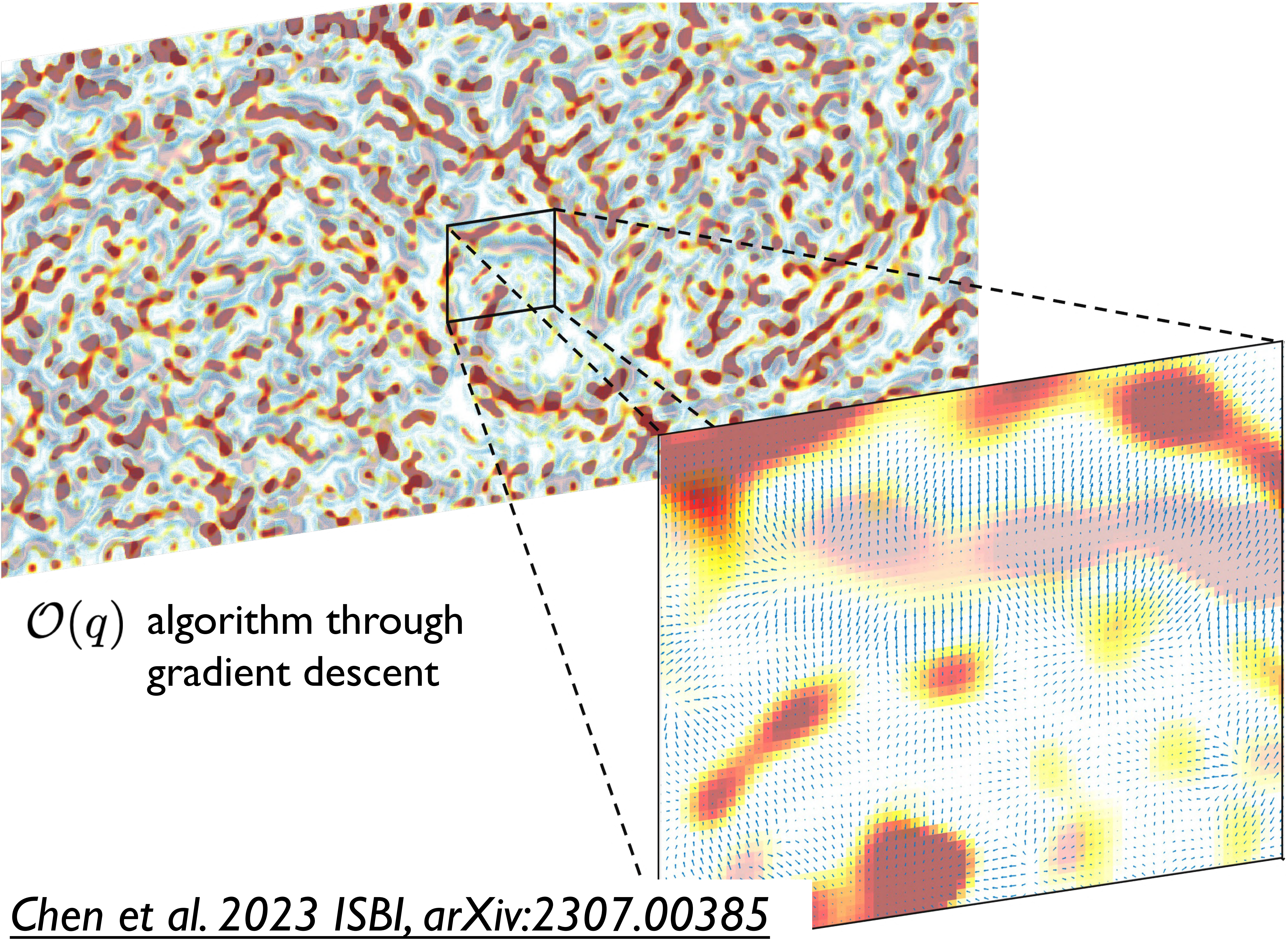
$$f_1(x) = \frac{1}{q}\sum_{i=1}^{q} \delta(x - x_i)$$

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

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

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

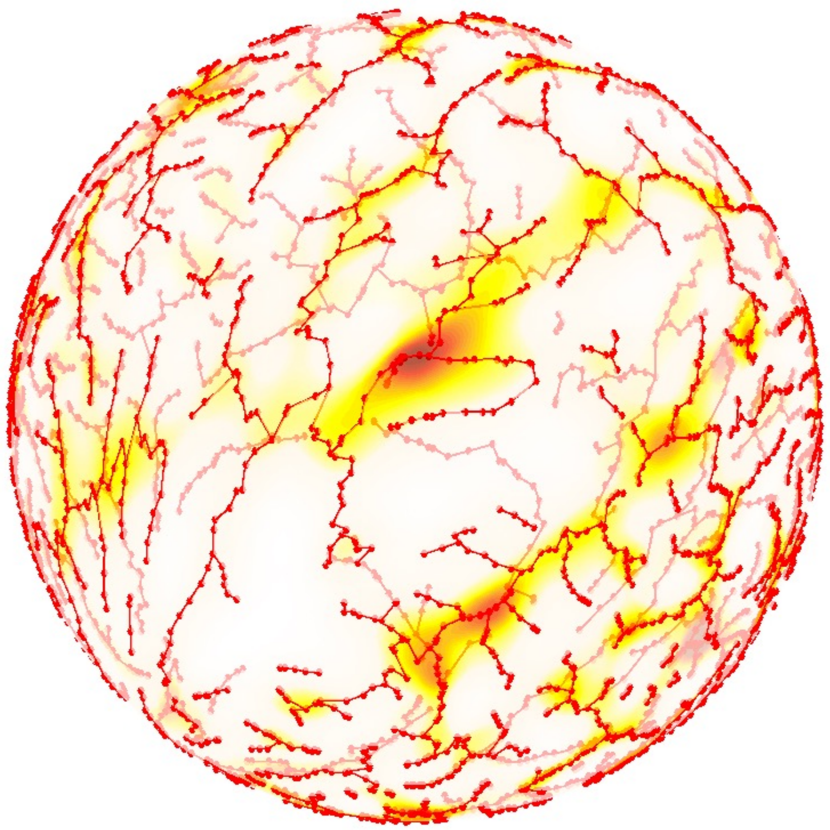
https://github.com/laplcebeltrami/sulcaltree

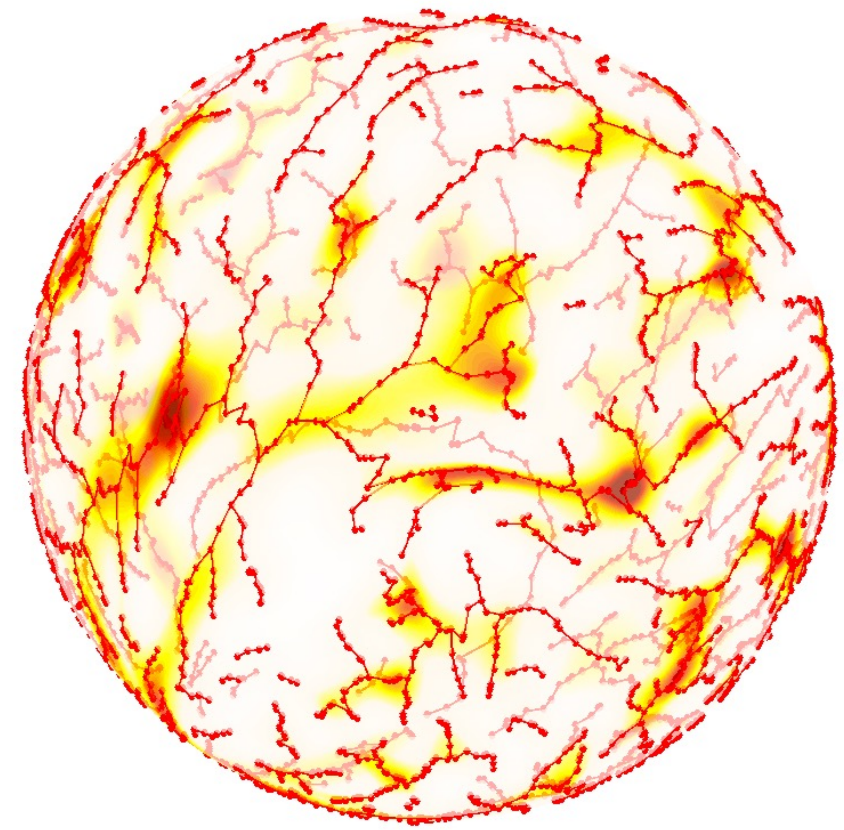


$\mathcal{O}(q)$ algorithm through gradient descent

<u>*Chen et al. 2023 ISBI, arXiv:2307.00385*</u>

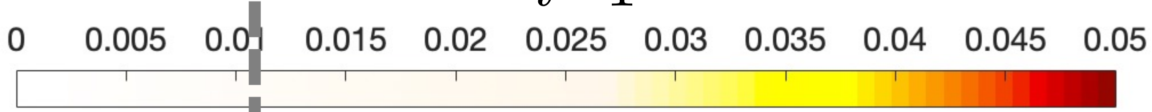
Theorem:
Invariance of Wasserstein distance on heat kernel smoothing

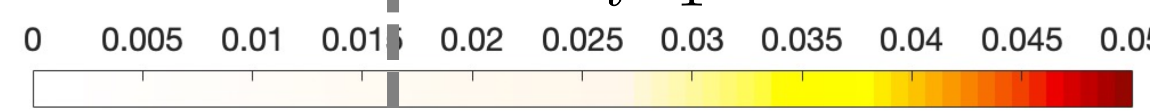




$$f_1(x) = \frac{1}{q}\sum_{i=1}^{q}\delta(x - x_i)$$

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





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

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

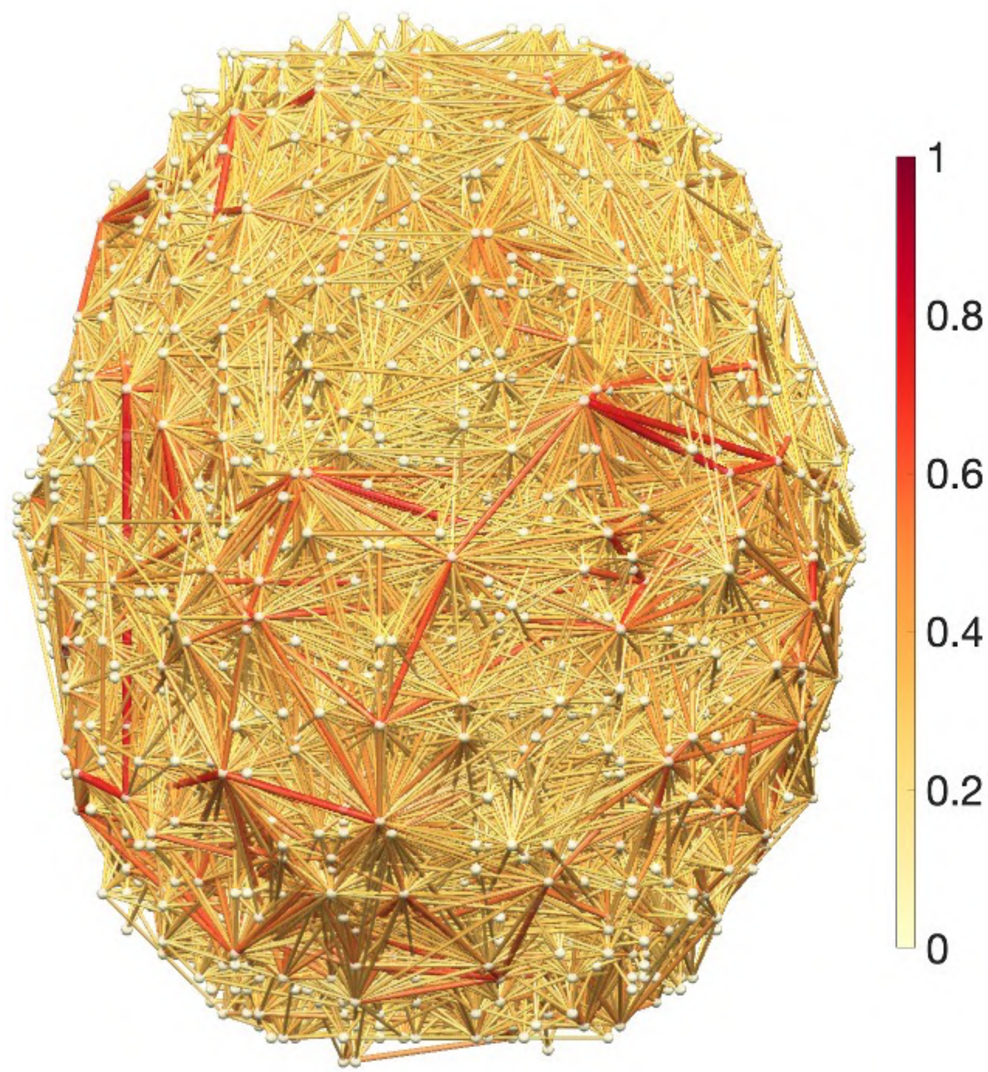
$$\mathcal{D}(f_1, f_2) = \mathcal{D}(K_\sigma * f_1, K_\sigma * f_2)$$

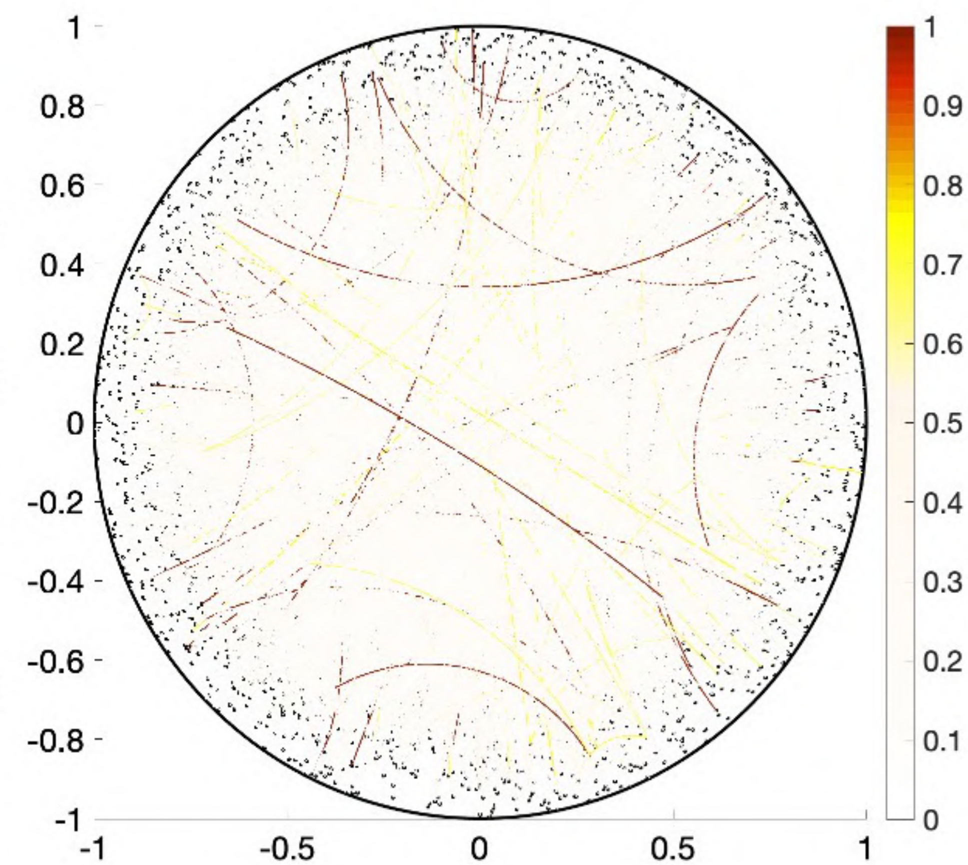
Chen et al. 2023 ISBI

Open research problem

Develop scalable algorithms for computing Wasserstein distance in other manifolds:

Space of positive definite symmetric matrices





Poincare disk

Chung and Chen 2022 arXiv: 2204.03653

Theorem: Wasserstein distance on graph filtrations

$$\mathcal{L}_{0D}(\Theta, P) = \min_{\tau} \sum_{b \in E_0} \big[b - \tau(b)\big]^2$$

Birth set

$$= \sum_{b \in E_0} \big[b - \tau_0^*(b)\big]^2$$

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

$$\mathcal{L}_{1D}(\Theta, P) = \min_{\tau} \sum_{d \in E_1} \big[d - \tau(d)\big]^2$$

Death set

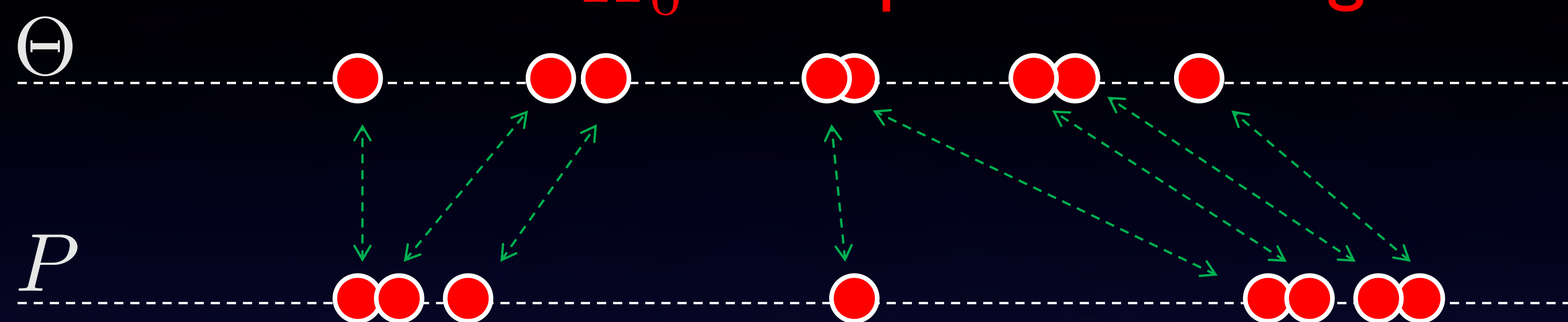
$$= \sum_{d \in E_1} \big[d - \tau_1^*(d)\big]^2$$

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

Songdechakraiwut and Chung. 2023, Annals of Appled Statistics arXiv: 2012.00675

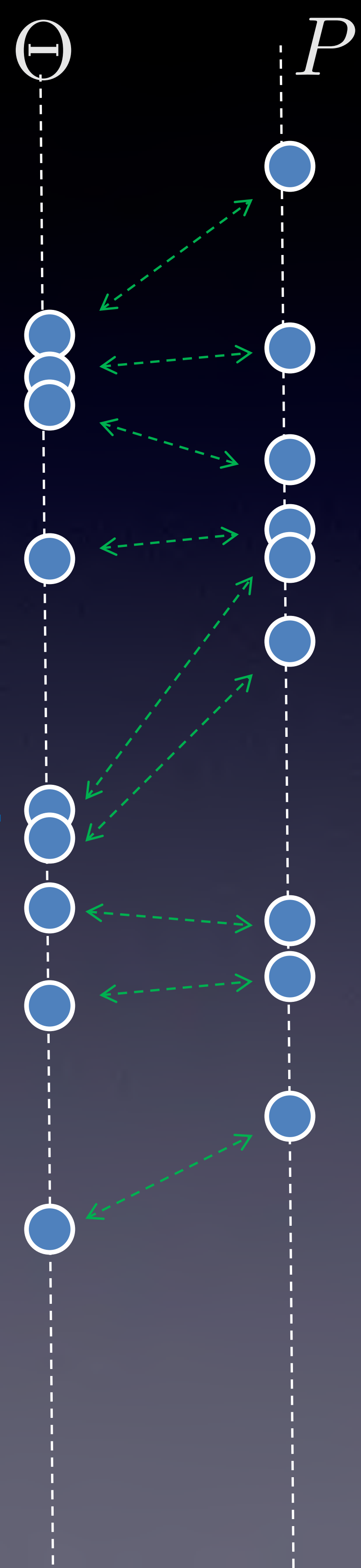
Wasserstein distance for graph filtrations

H_0 0D persistent diagram



H_1

1D persistent diagram



1D assignment problem has known analytic solution

$\mathcal{O}(q \log q)$

Topological ~~Inference~~ *Clustering*

distance-based inference (our approach)

vs.

trditional feature-based inference

Songdechakraiwut and Chung 2023 Annals of Appled Statistics
Chung et al. 2023 arXiv:2201.00087

Ratio statistic for Wasserstein distances

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

Between-group distance

$$l_B \propto \sum_{i \in C_1, j \in C_2} \mathcal{L}(\mathcal{X}_i, \mathcal{X}_j)$$

← 0D, 1D and combined distances

Within-group distance

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

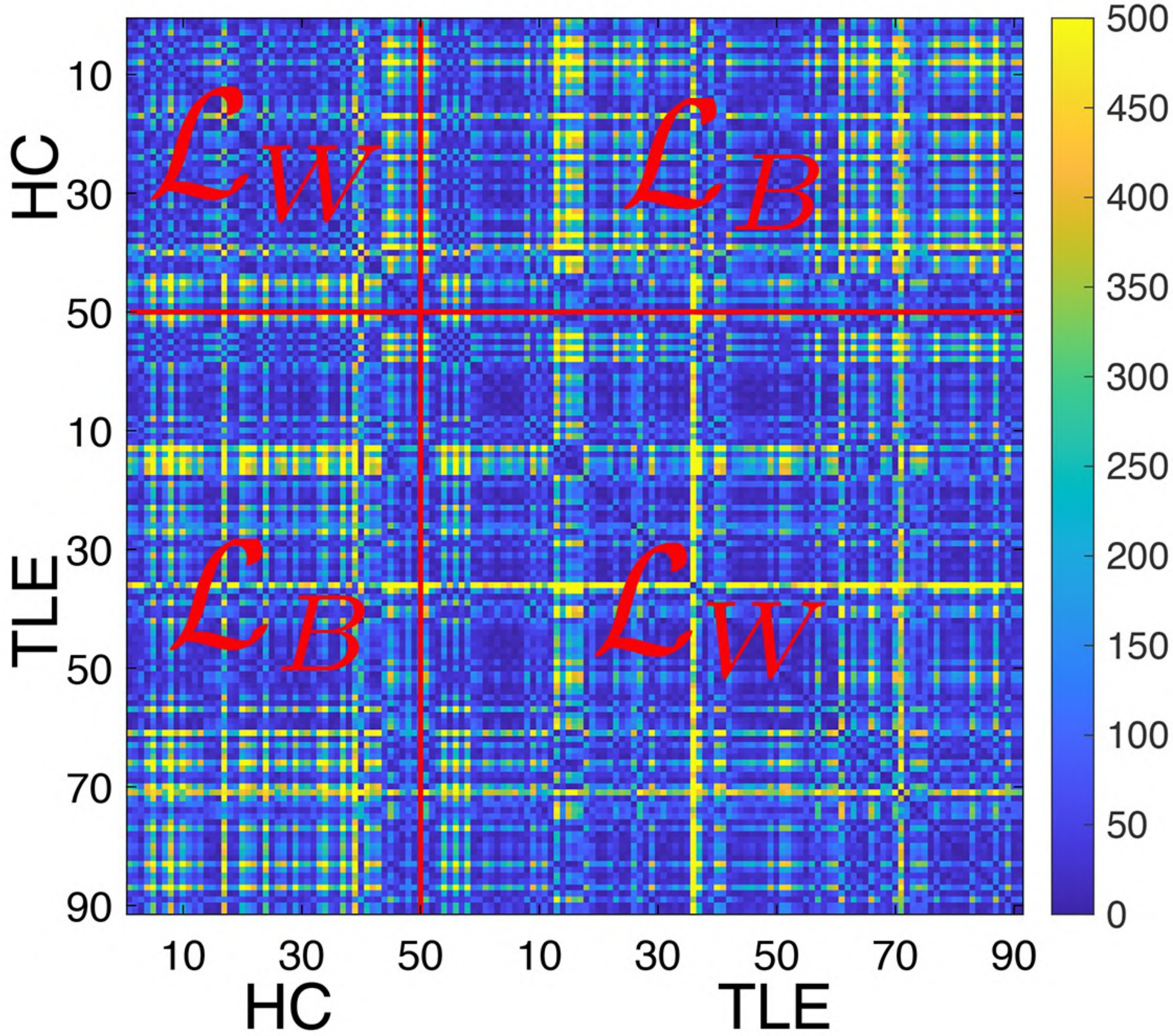
→ Statistic $\phi = \frac{l_B}{l_W}$

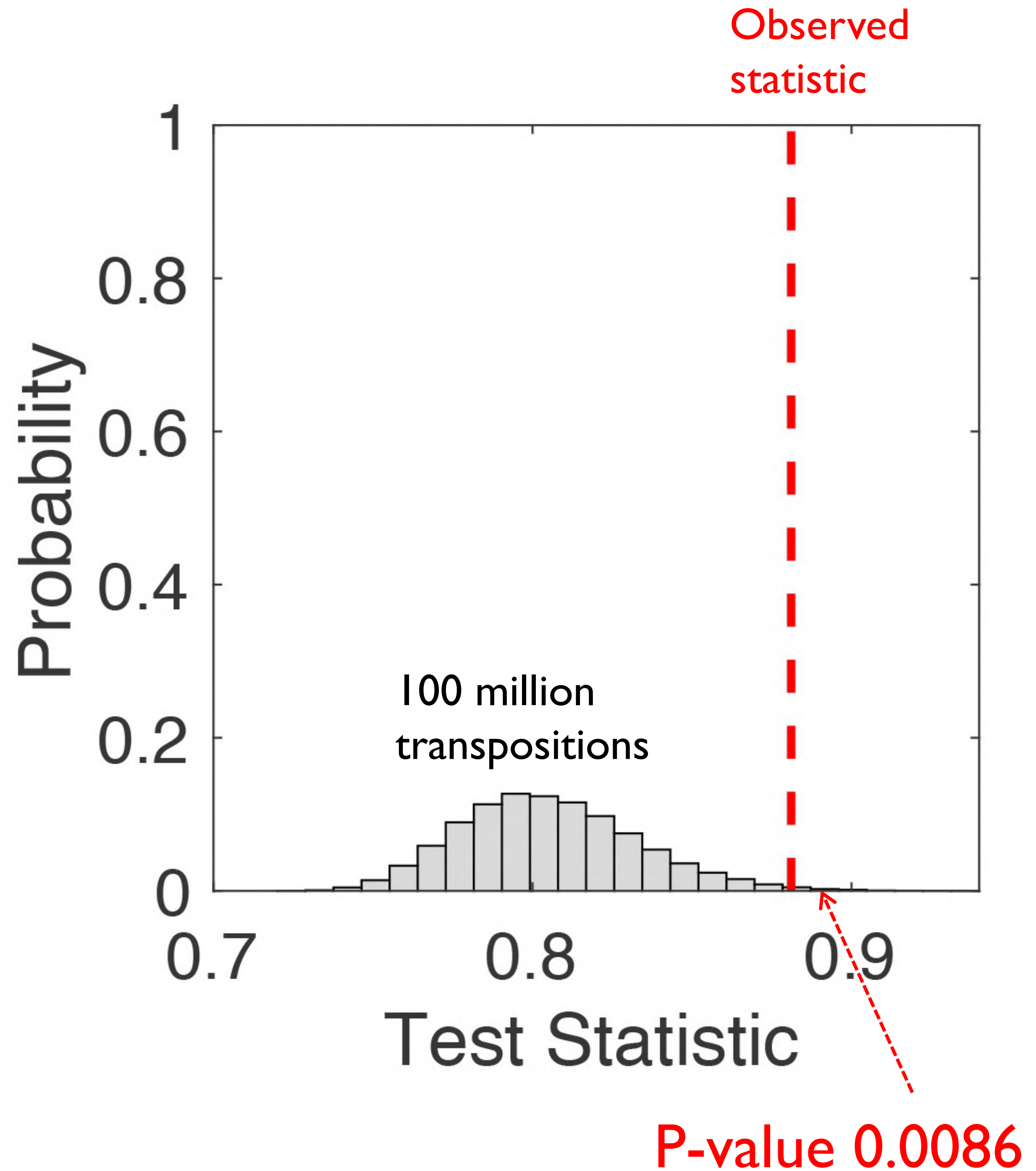
Small ϕ → small group separation

Large ϕ → large group separation

More complex ANOVA-type inference can be easily done

Online permutation test on pairwise distance matrix





$$l_W \rightarrow l_W + \Delta(tranposition)$$

$$l_B \rightarrow l_B + \Delta(tranposition)$$

Songdechakraiwut and Chung 2023
Annals of Appled Statistics

Topological clustering

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

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

Geometric proof: arXiv:2201.00087

Geometry of Wasserstein distance

Birth values are points in the convex polytope

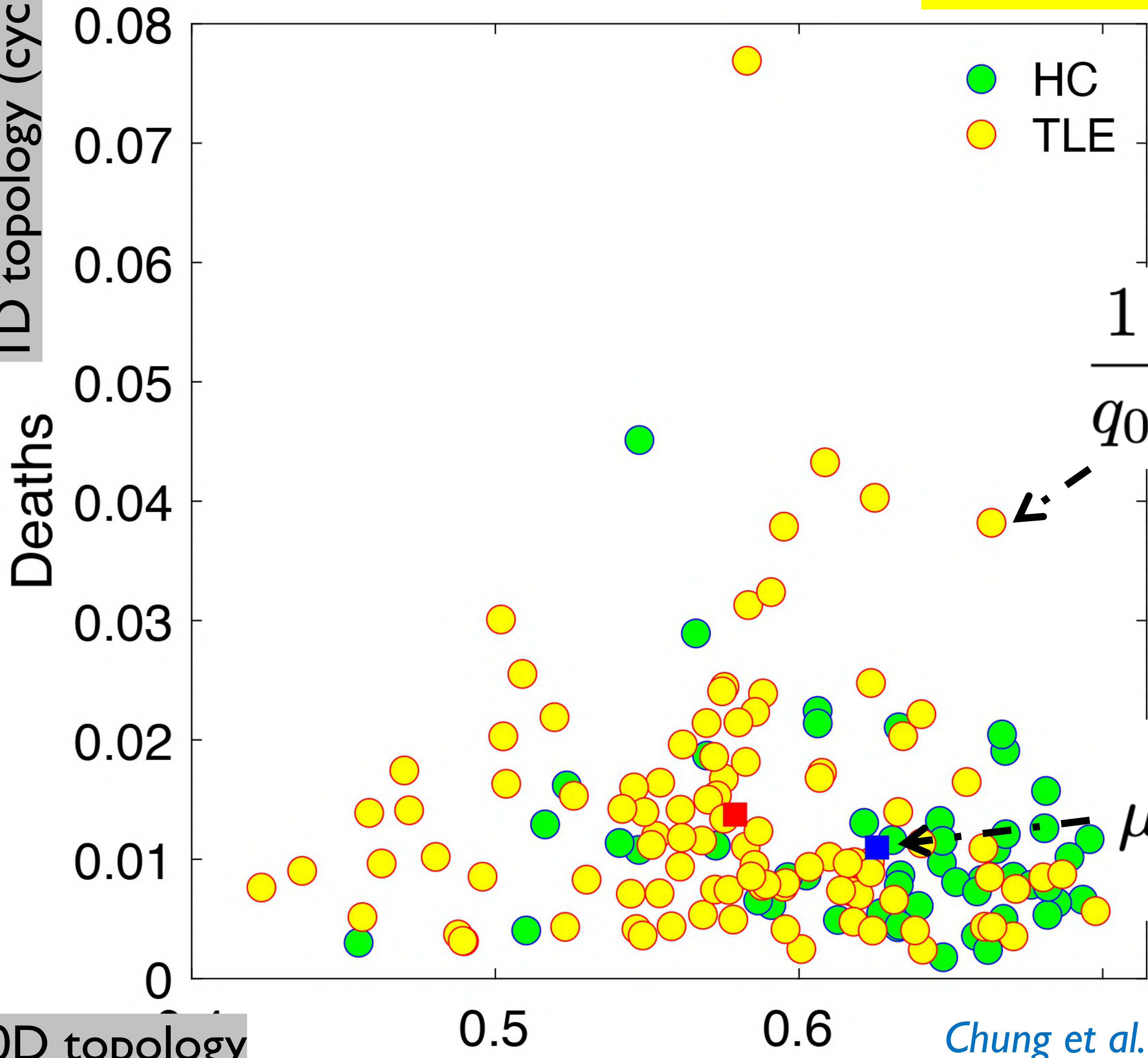
$$\mathcal{T}_0 = \{(x_1, x_2, \cdots, x_{q_0}) | x_1 < x_2 < \cdots < x_{q_0}\} \subset \mathbb{R}^{q_0}$$

Death values are points in the convex polytope

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

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

Birth-death embedding



1D topology (cycles)

0D topology (connected components)

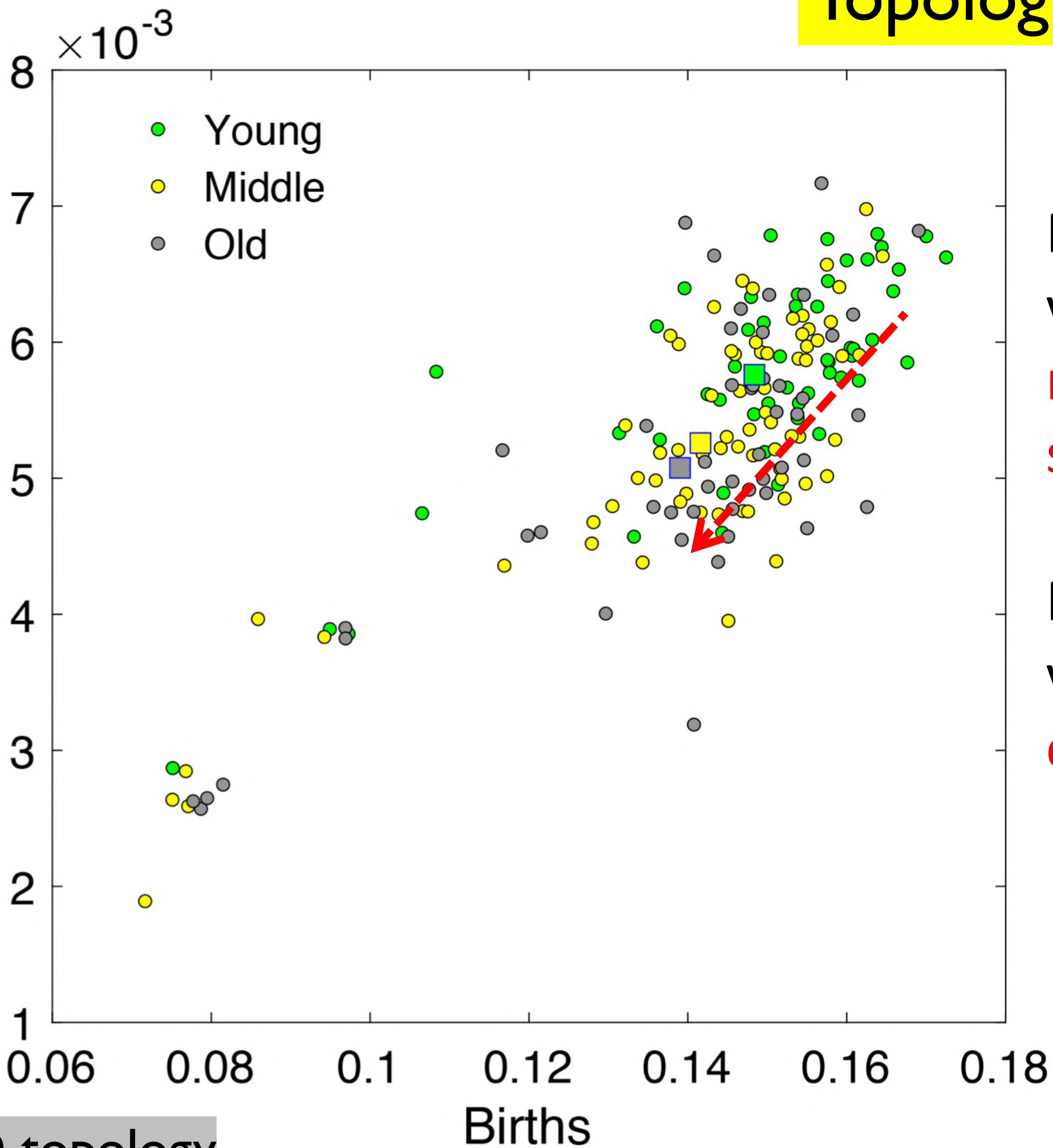
i-th subject

$$\frac{1}{q_0}\sum_{k=1}^{q_0}(b_{(i)}^k - \mu_b)$$

$$\mu_b = \frac{1}{q_0}\sum_{k=1}^{q_0} b_{(i)}^k$$

Chung et al. 2023 arXiv:2302.06673
under review in NeuroImage

Topological gradient in aging



1D topology (cycles)

0D topology (connected components)

Decreasing birth values →
more disconnected subnetworks

Decreasing death values →
cycles are disappearing

Joint work with James Gee of University of Pennsylvania

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

New simplicial complex data structure for brain networks

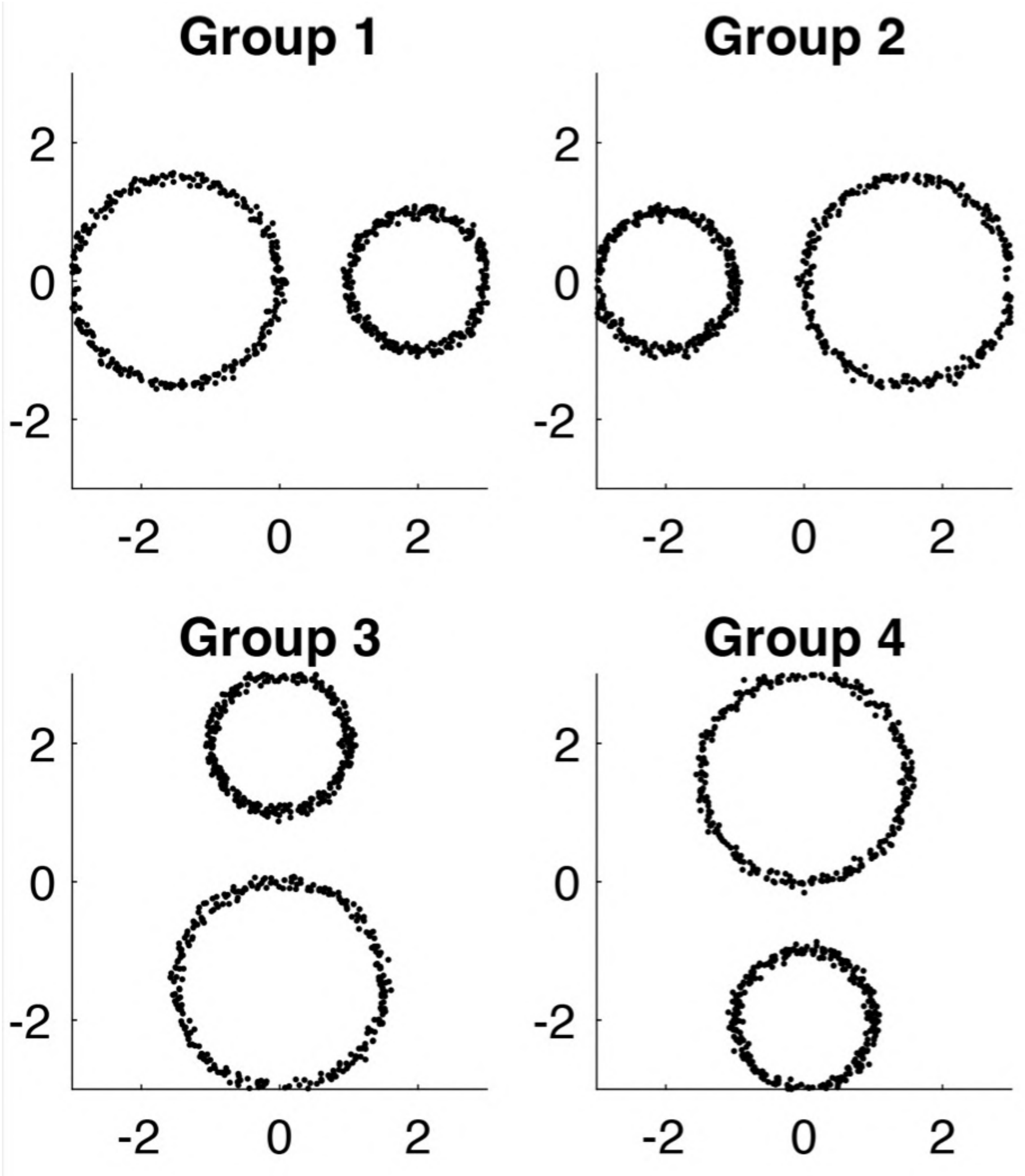
Structured/cell array can handle variable length data.

```
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

$\sigma = 0.05$



All false positives

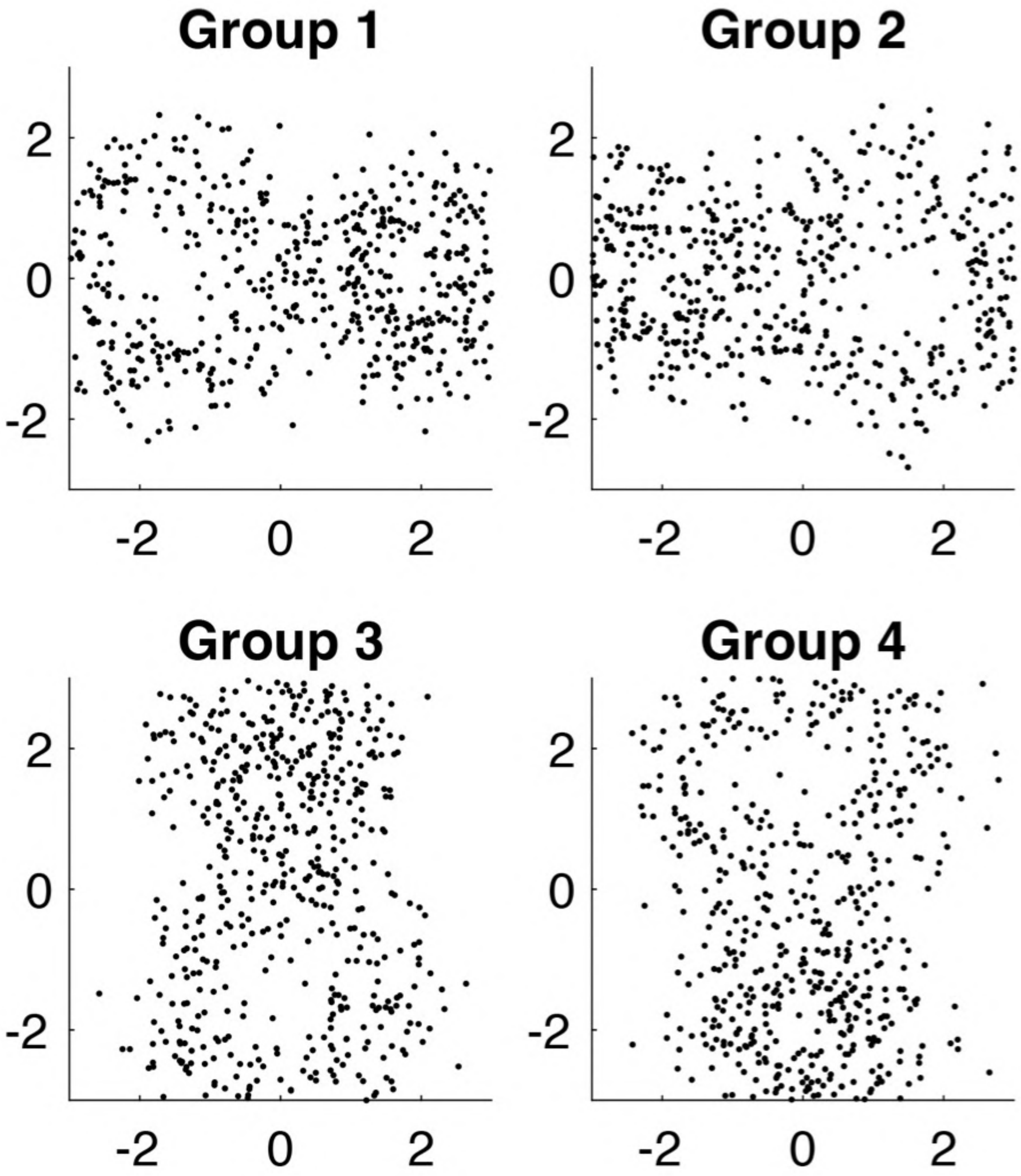
K-means clustering
0.98 +- 0.01

Hierarchical clustering
1.00 +- 0.00

Topological clustering
0.63 +- 0.04

Testing if we are detecting topological false positives

$\sigma = 0.5$



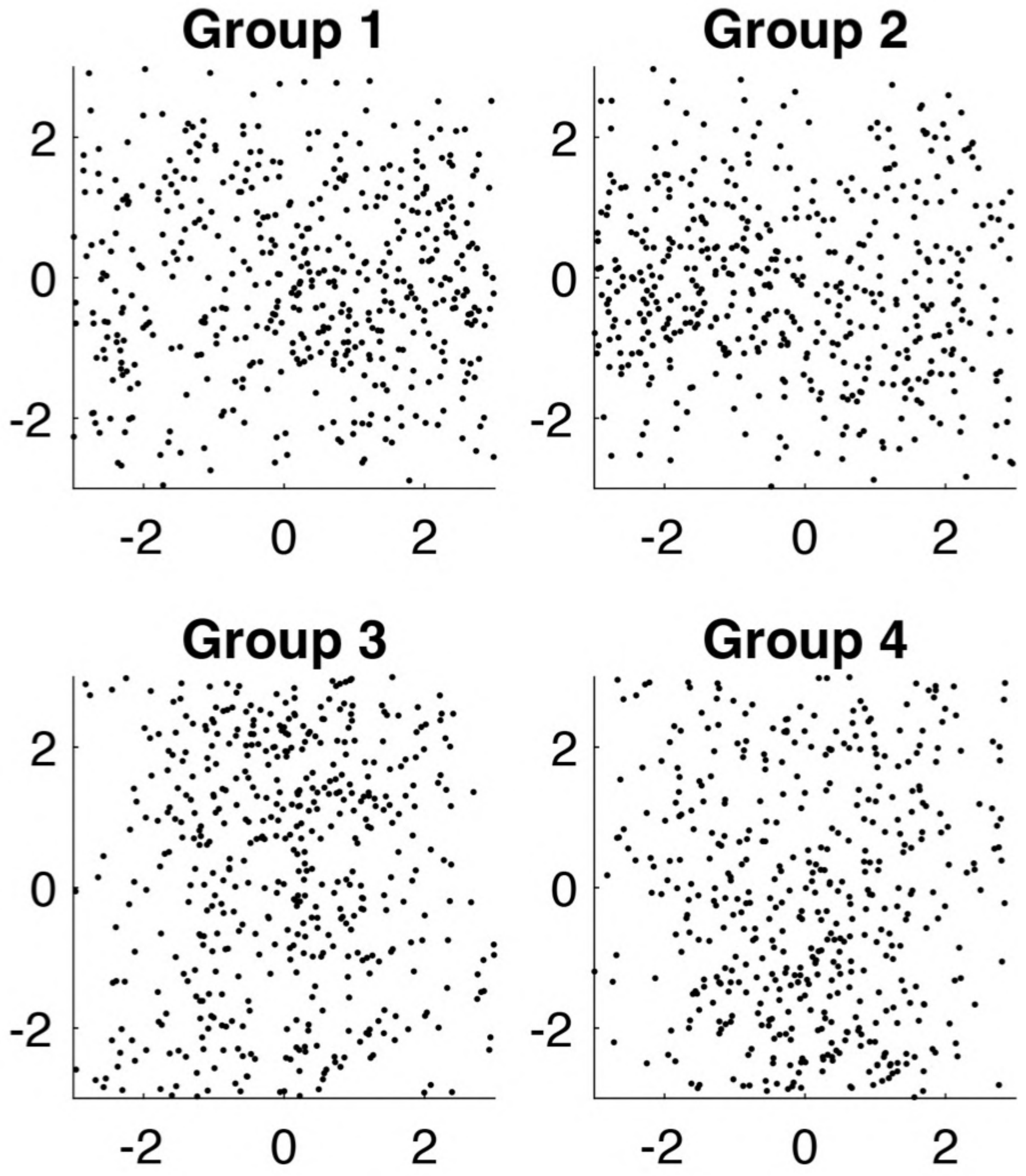
K-means clustering
0.81 +- 0.02

Hierarchical clustering
1.00 +- 0.00

Topological clustering
0.44 +- 0.04

Testing if we are detecting topological false positives

$\sigma = 1.0$



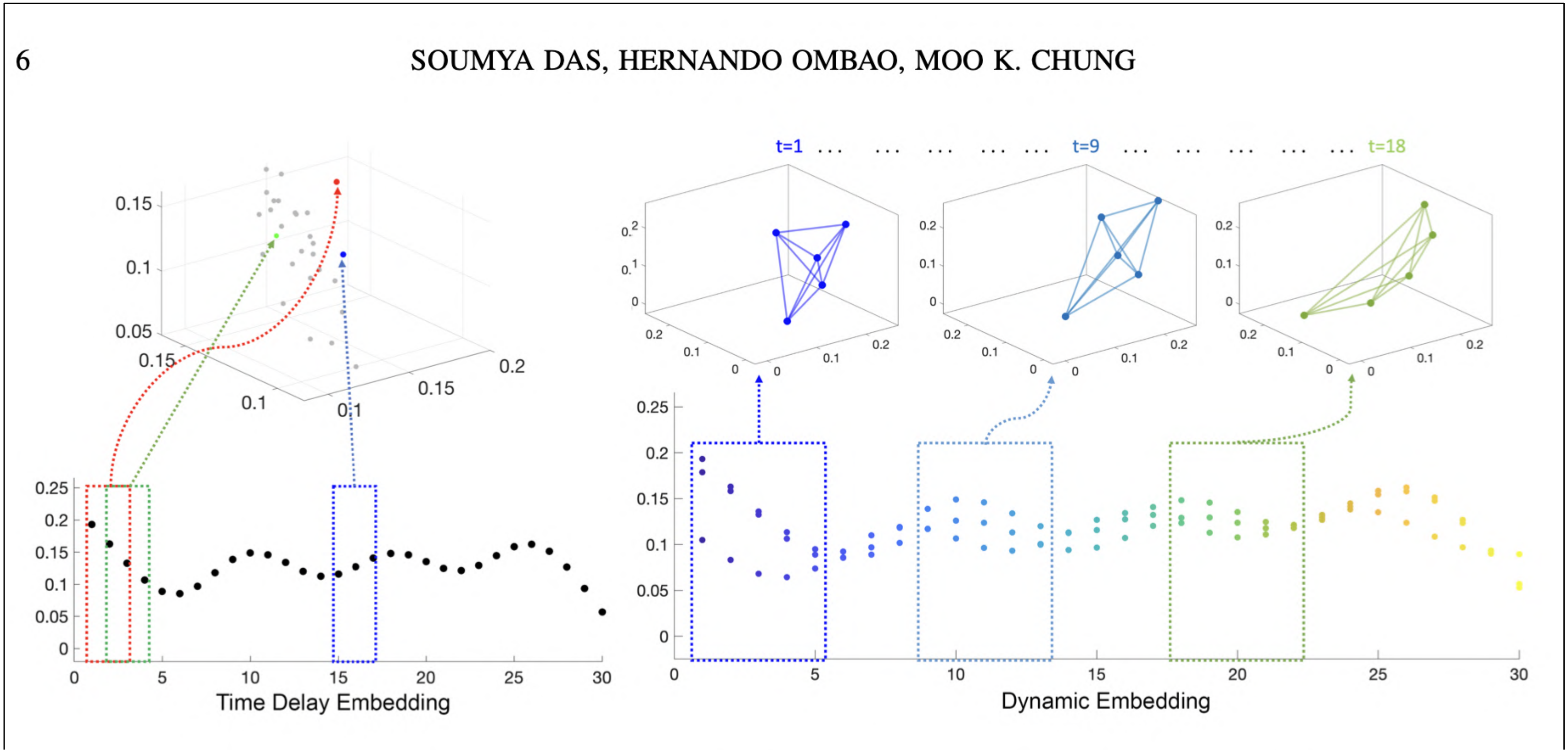
K-means clustering
0.70 +- 0.02

Hierarchical clustering
0.91 +- 0.08

Topological clustering
0.43 +- 0.04

Results

Open research problem: Embedding of time series data

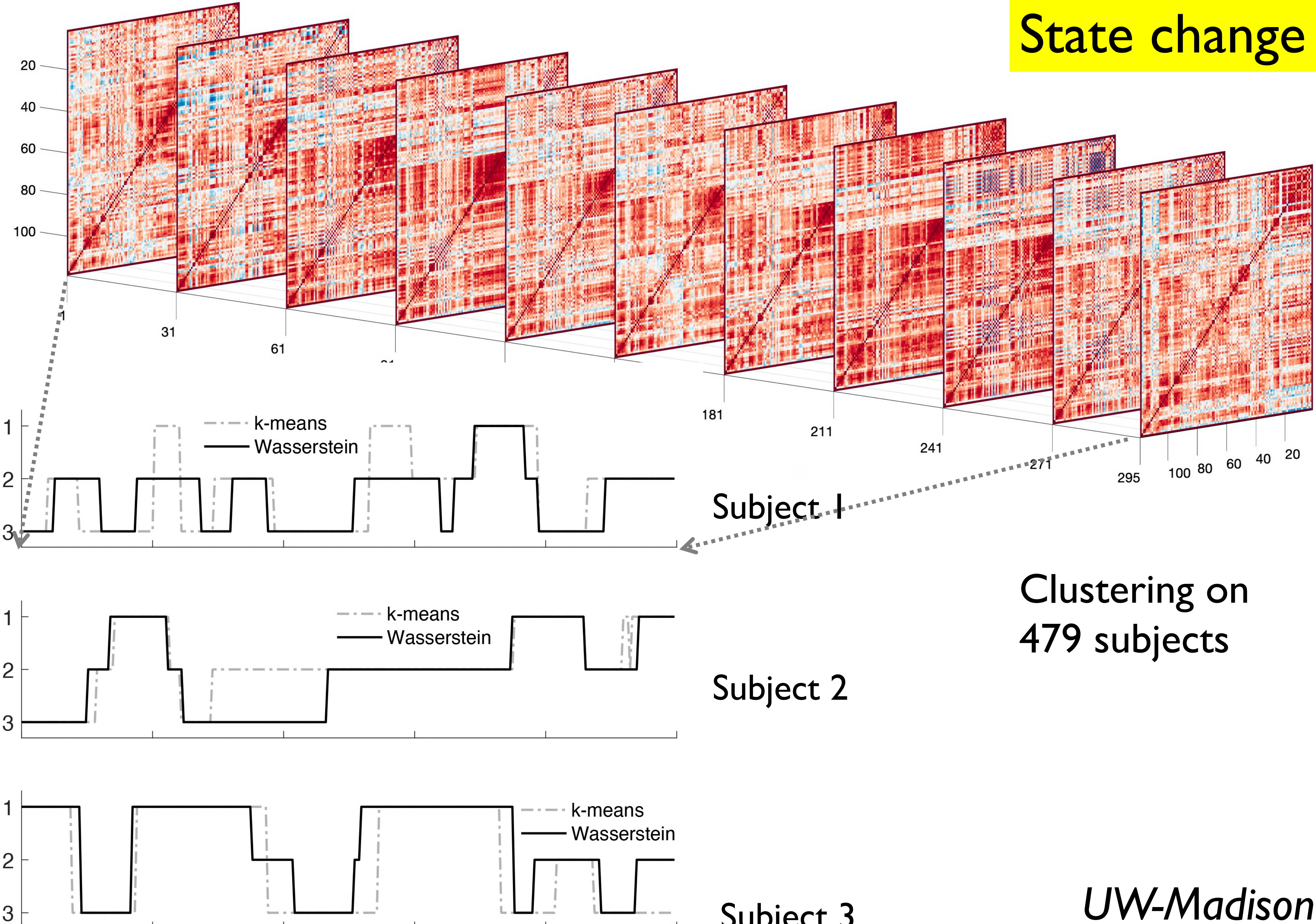


Das et al. 2022 arXiv:2210.09092

Under review in Foundations of Data Science

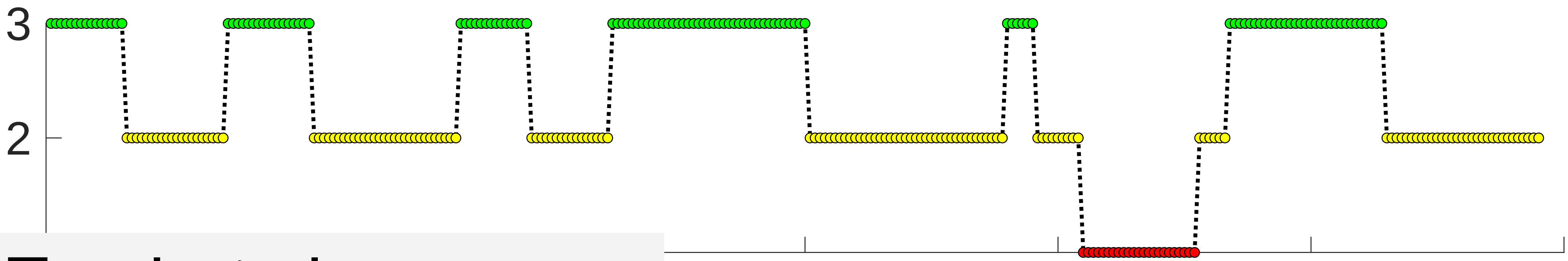
Journal has the heaviest concentration of TDA experts in the editorial board

State change

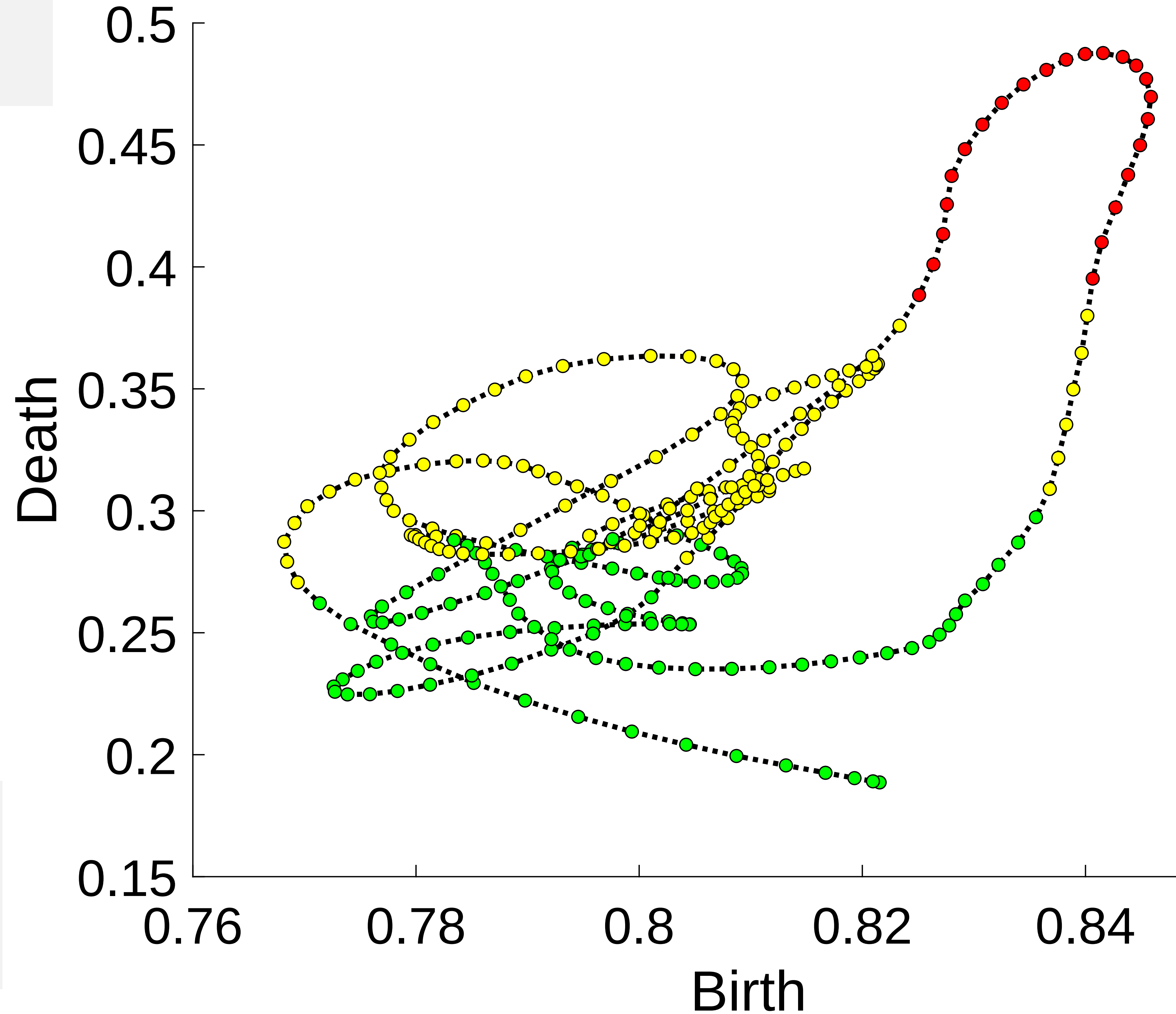


Clustering on 479 subjects

UW-Madison Twin study

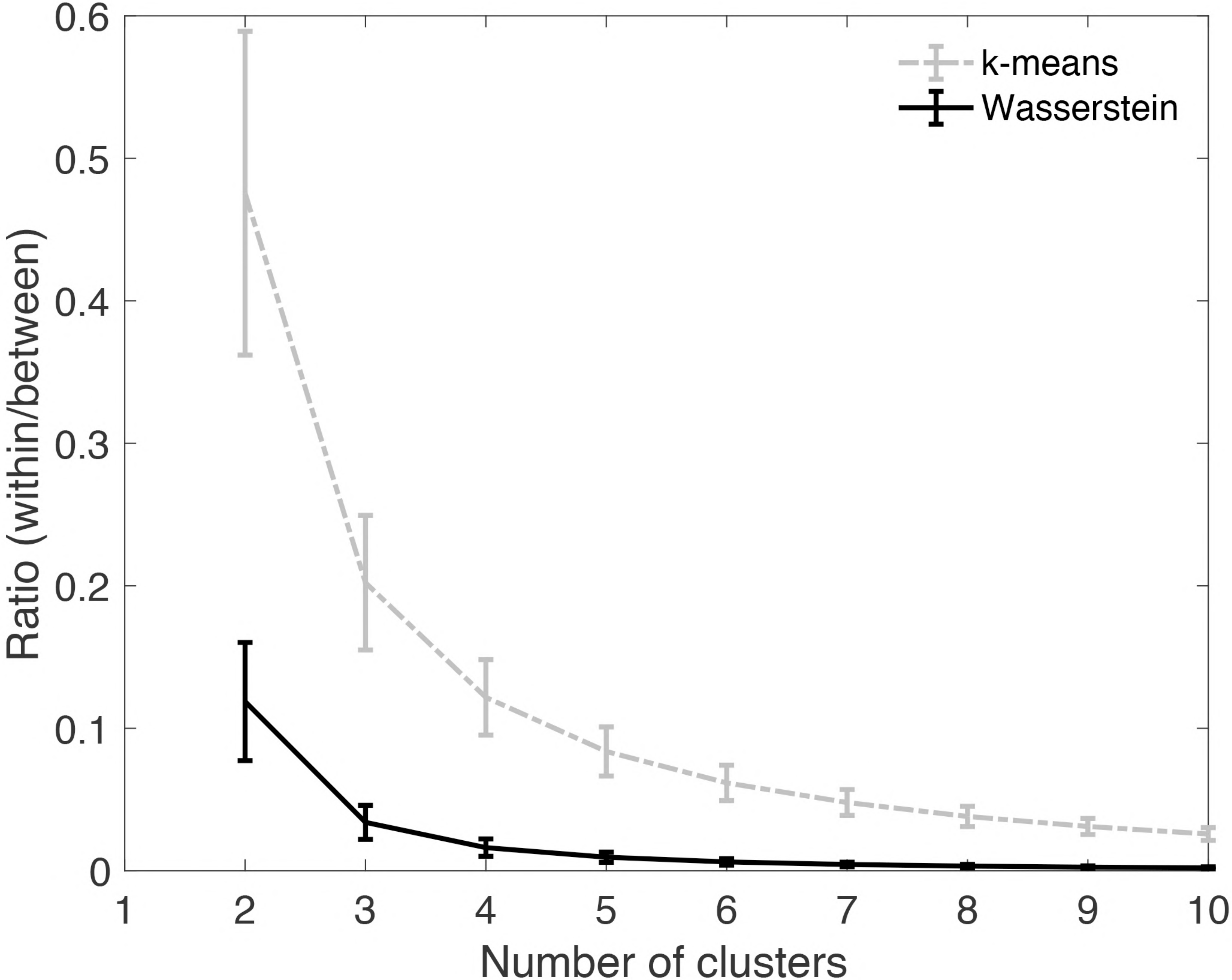


Topological state space estimation



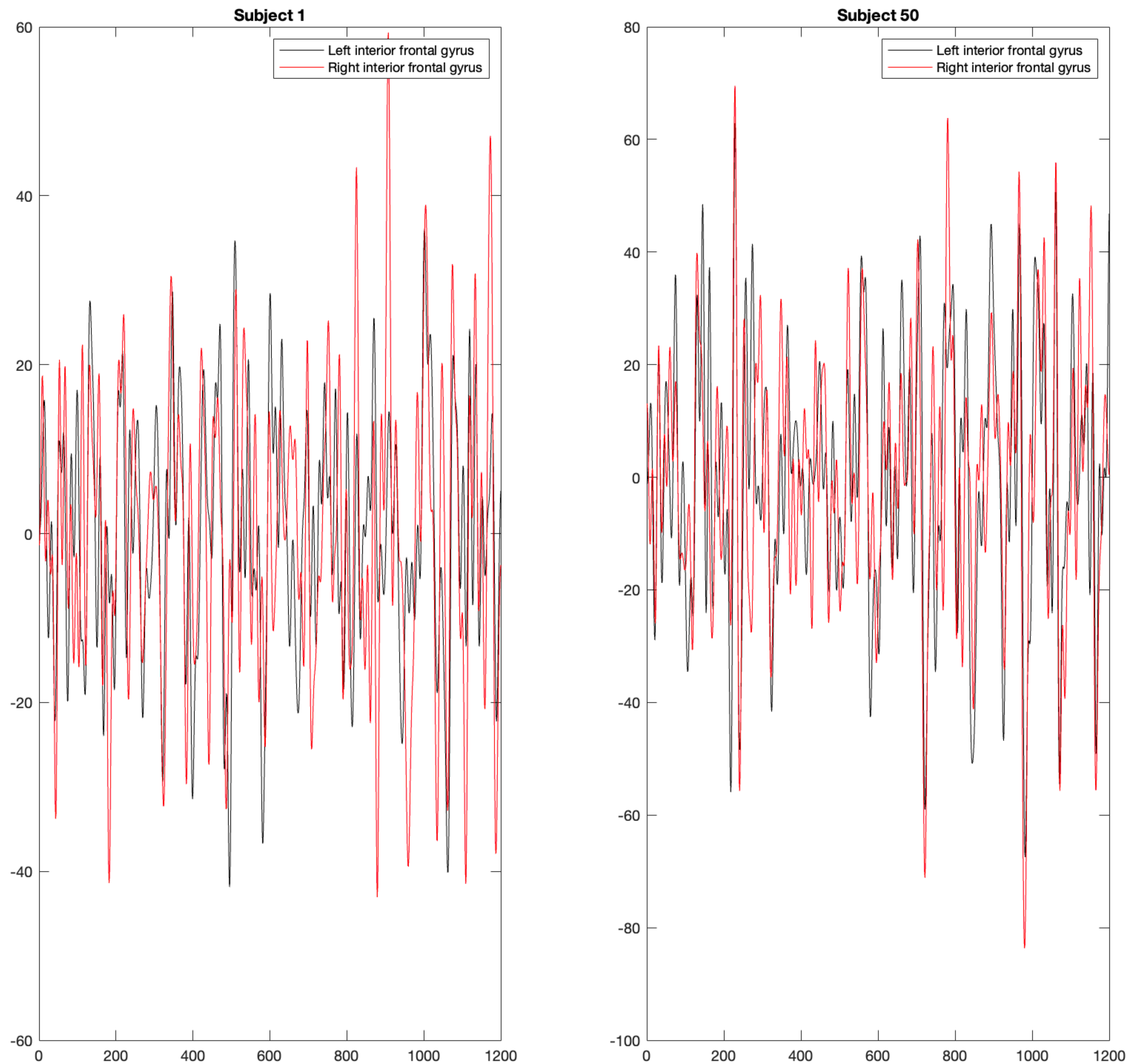
Topological embedding

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



The within cluster variance *6 times* smaller

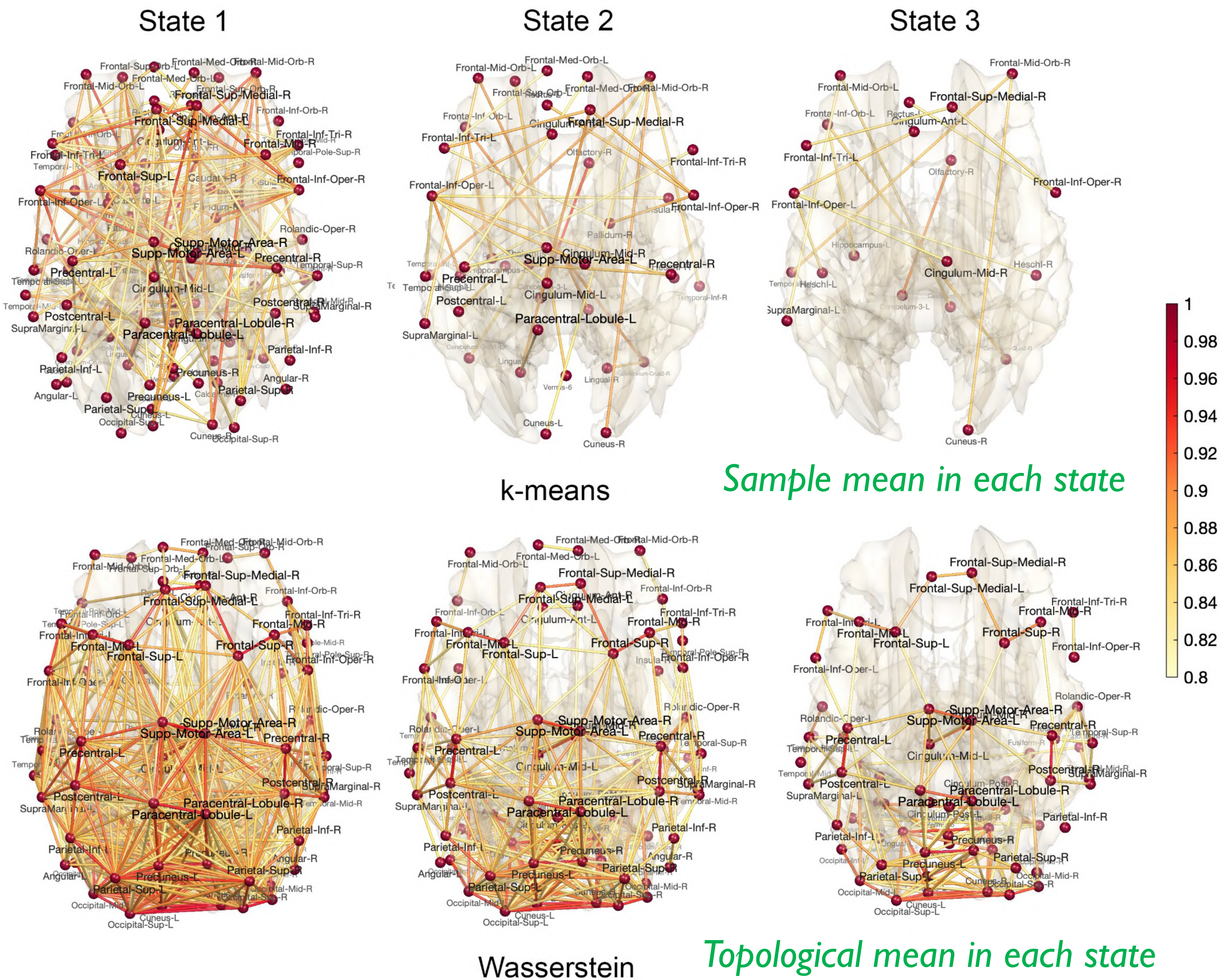
Open research problem



How to do a joint clustering of paired time series?

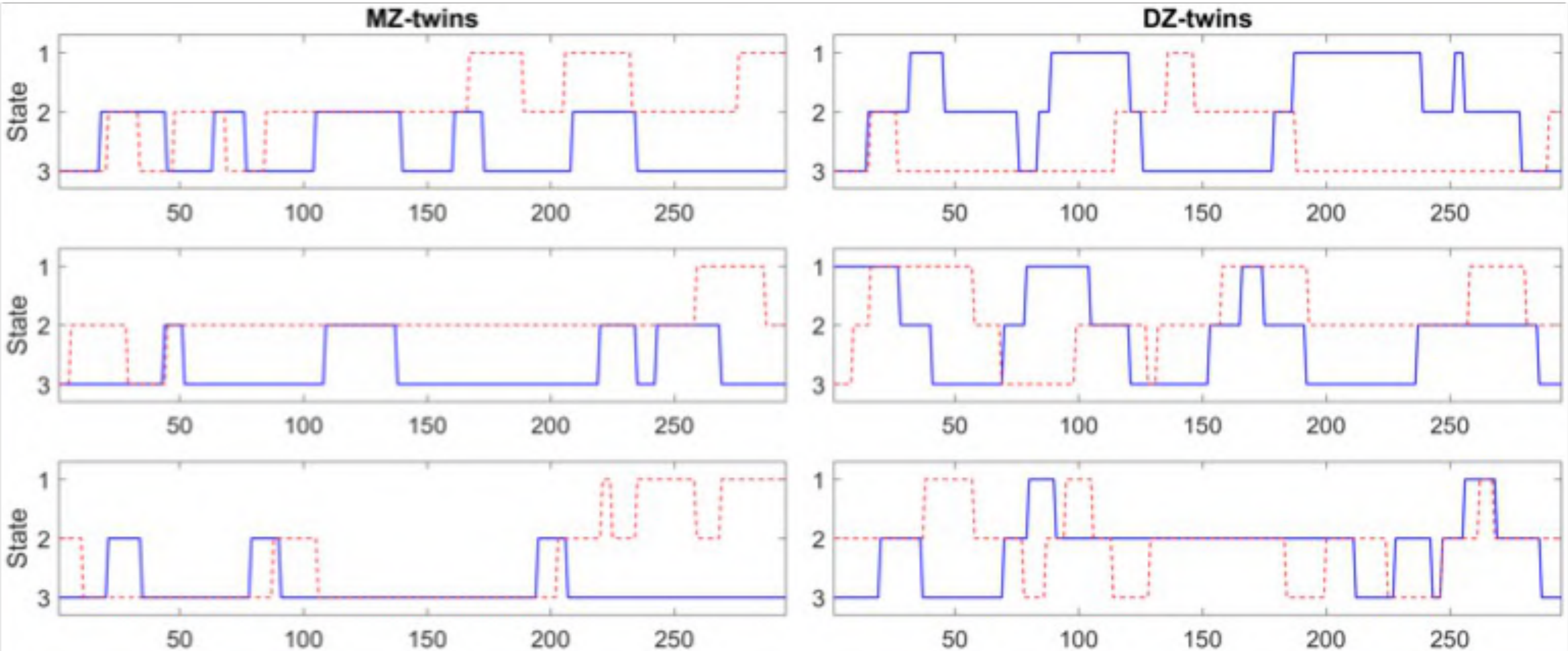
Is the estimated state space periodic?

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

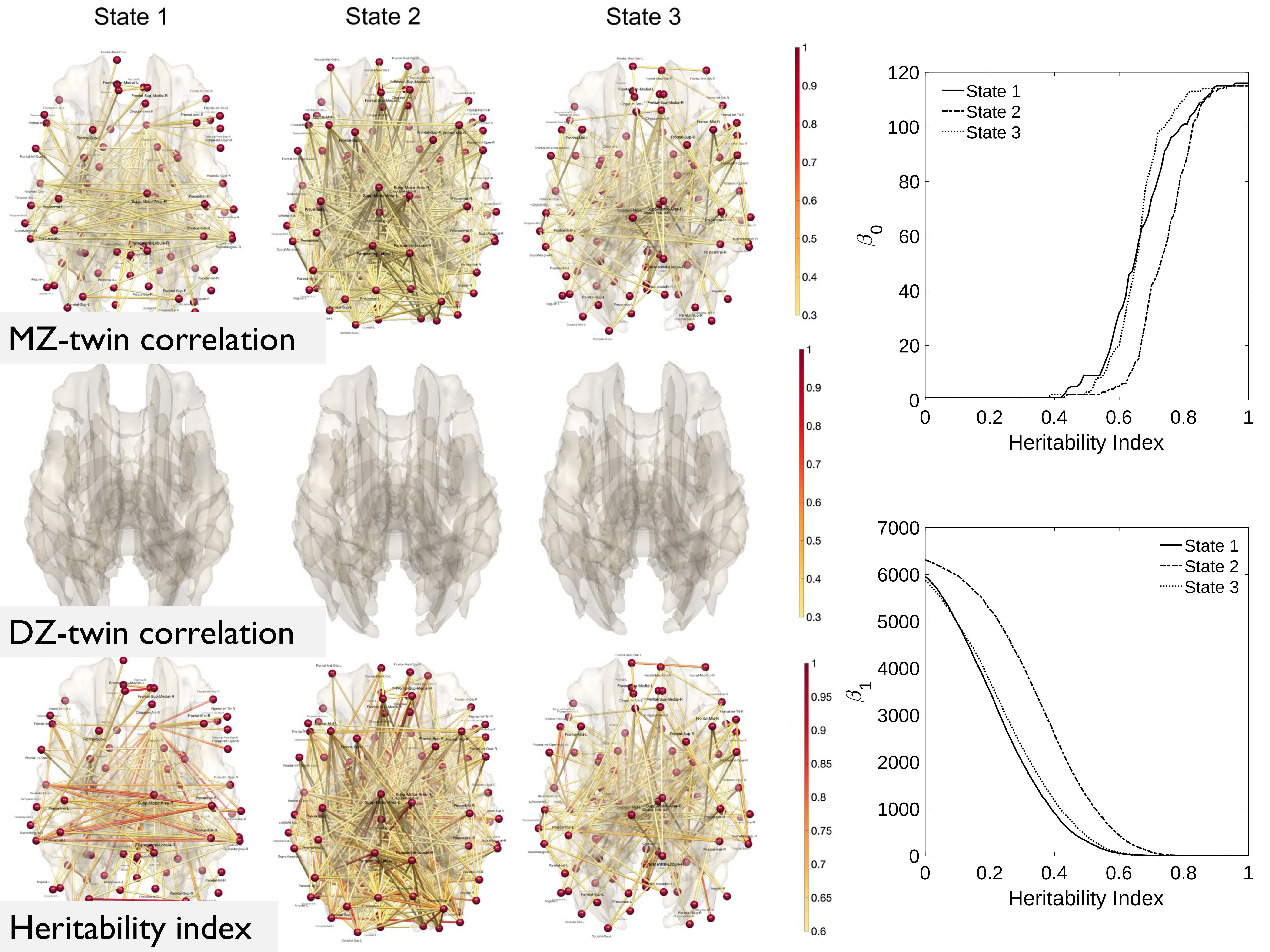


State space estimation on 479 subjects

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
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
1
0.95
0.9
0.85
0.8
0.75
0.7
0.65
0.6
β_0
β_1
Heritability Index
Heritability Index
State 1
State 2
State 3
0
20
40
60
80
100
120
0
1000
2000
3000
4000
5000
6000
7000
0
0.2
0.4
0.6
0.8
1

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+ attendence

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.


We are located here. Join us for
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if you are better than chat-GPT