Tutorial 6 pt I: Topological Data Analysis for Biomedical Imaging Data

Thu, Apr 20, 11:30 – 13:00

SALÓN BARAHONA 2

Tutorial 6 pt II: Topological Data Analysis for Biomedical Imaging Data

Thu, Apr 20, 16:00 – 17:30

SALÓN BARAHONA 2

You can d/l all the lecture materials and codes from

https://github.com/laplcebeltrami/ISBI2023TDA

The Waisman Laboratory for Brain Imaging and Behavior

University of Wisconsin SCHOOL OF MEDICINE AND PUBLIC HEALTH

Lecture 1 Simplicial homology and persistent homology

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https://github.com/laplcebeltrami/ISBI2023TDA

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Matlab toolbox PH-STAT

Statistical Inference on Persistent Homology

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

Chung 2023, PH-STAT arXIv:2304.05912

The codes are used to publish in leading journals and conferences since 2009: IEEE Transactions on Medical Imaging, NeuroImage, Human Brain Mapping, Annals of Applied Statistics, Information Processing in Medical Imaging (IPMI), MICCAI, ISBI

`WS_cluster.m` `PH_hodge_betti.m`

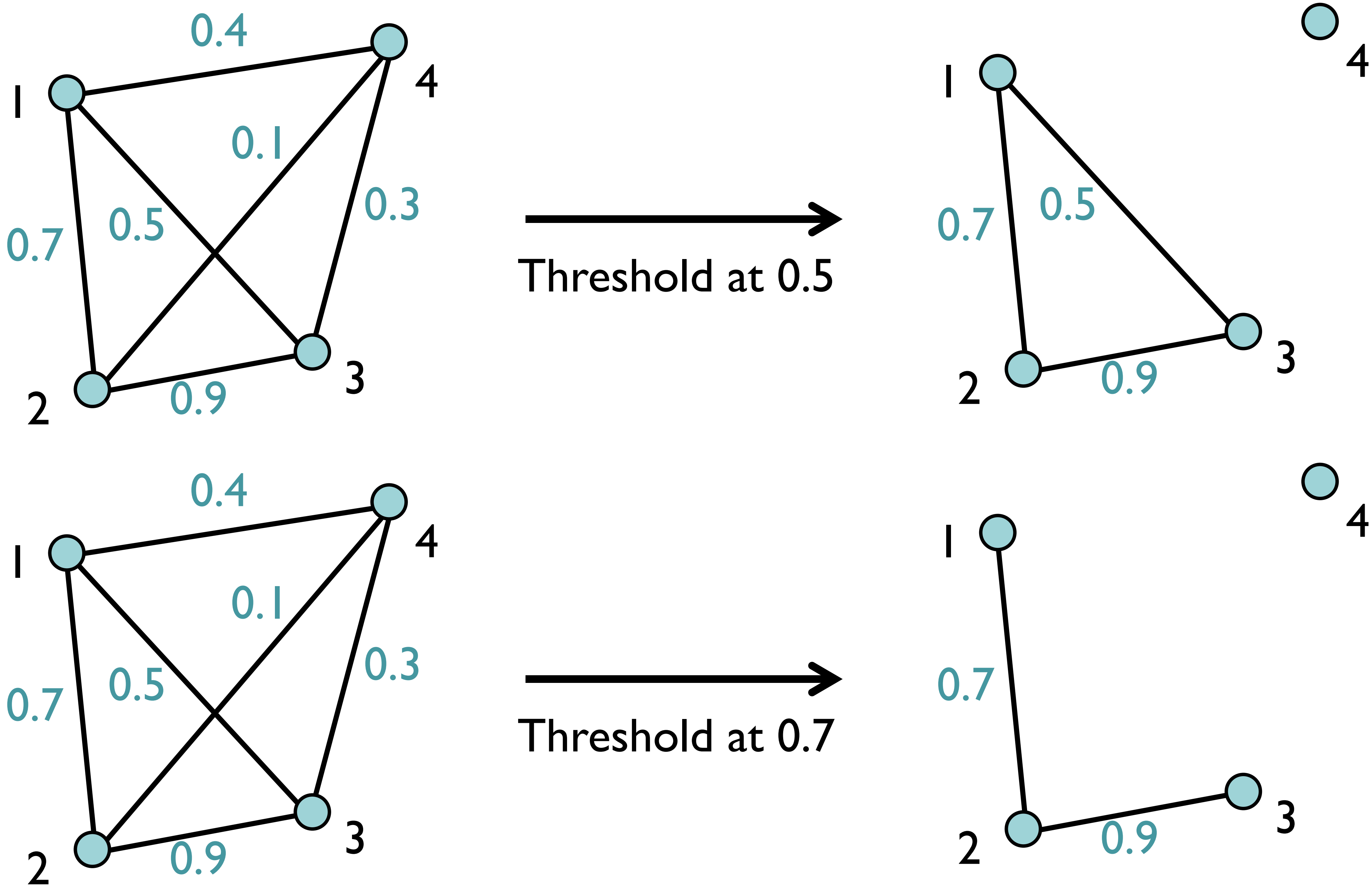
Persistent Homology

- Study properties of data that remain invariant under continuous transformations
- Captures the topological features of data across different scales
- More persistent topological features → signal
- Less persistent topological features → noise
- Multiscale approach

What is wrong with standard brain network analysis?

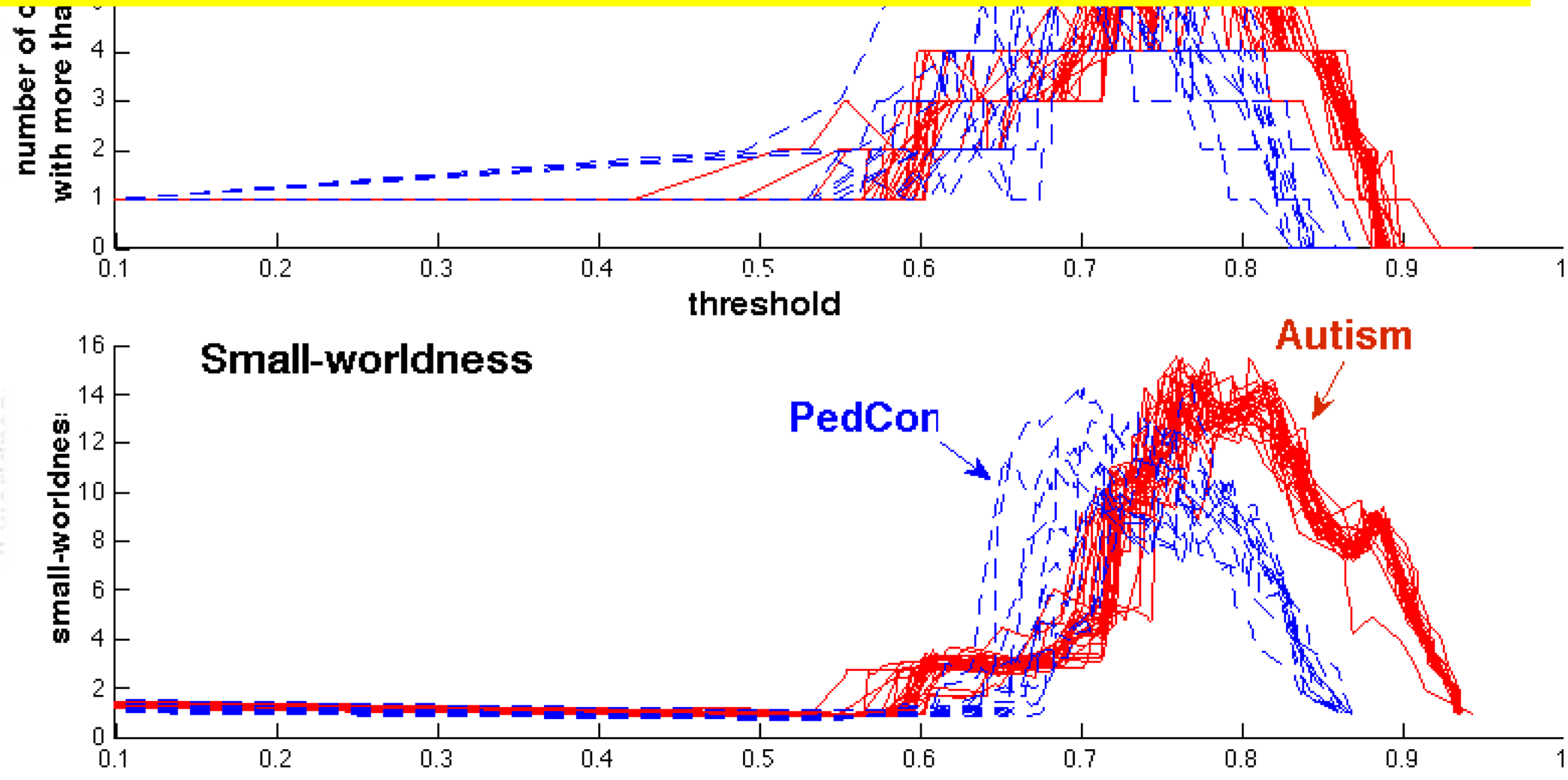
Edge weight ρ_{ij} between node *i* and *j*

→ Connectivity matrix $\rho = (\rho_{ij})$



Single threshold often suboptimal → multiple thresholds

What if we use every possible threshold → persistent homology



Lee et al. 2011. IEEE TMI 30:1154-1165

Betti numbers β_i

of i-dimensional holes/loops

β_0 = # of connected components = 3

β_1 = # of 1D holes = 1

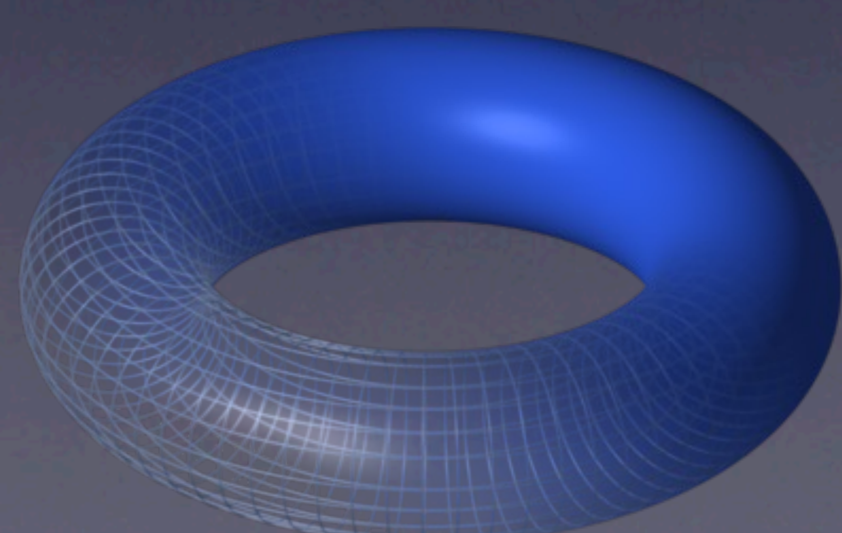
β_2 = # of 2D cavities =0

Betti-number representation:

(3,1,0,0,…)

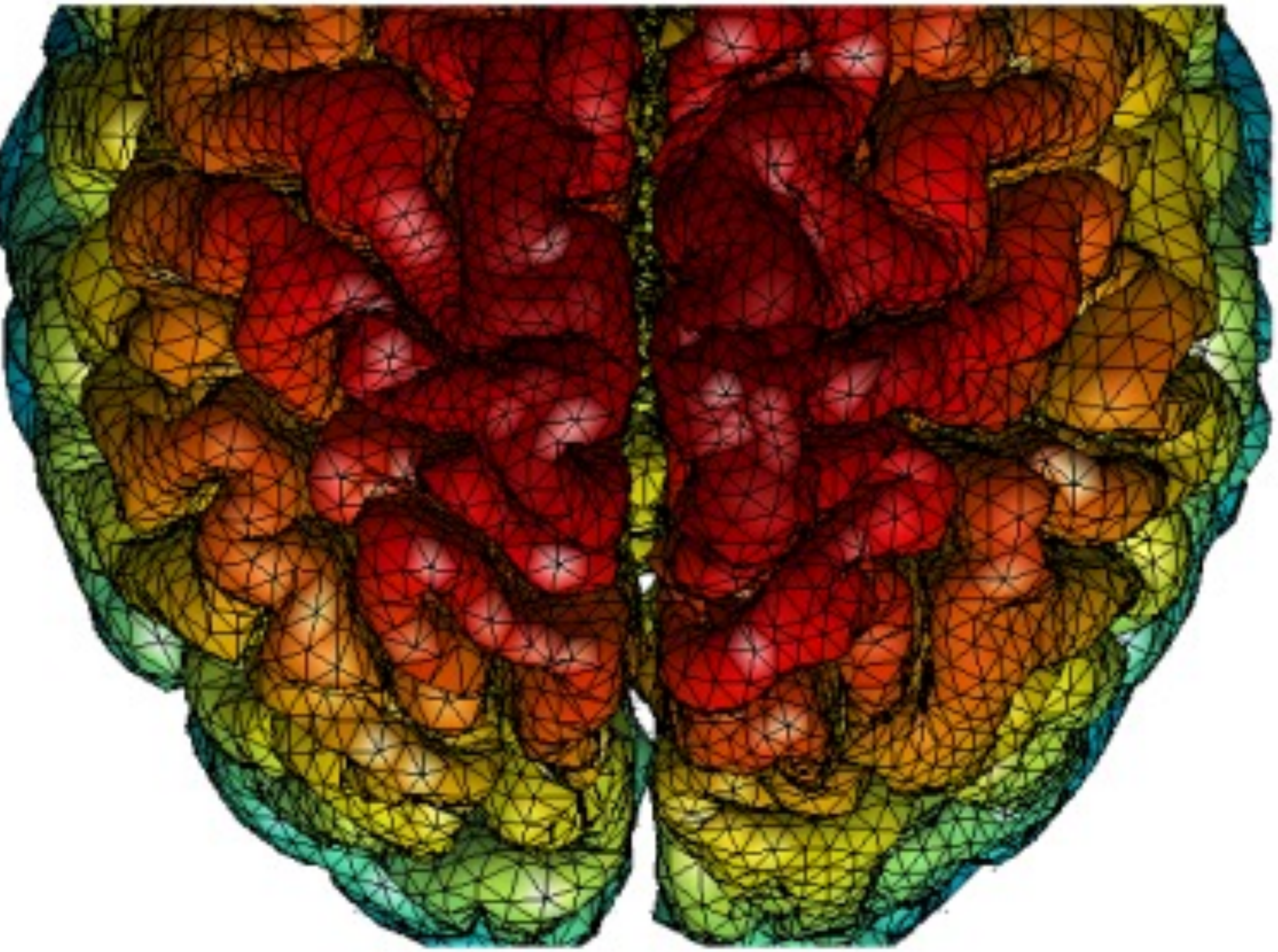
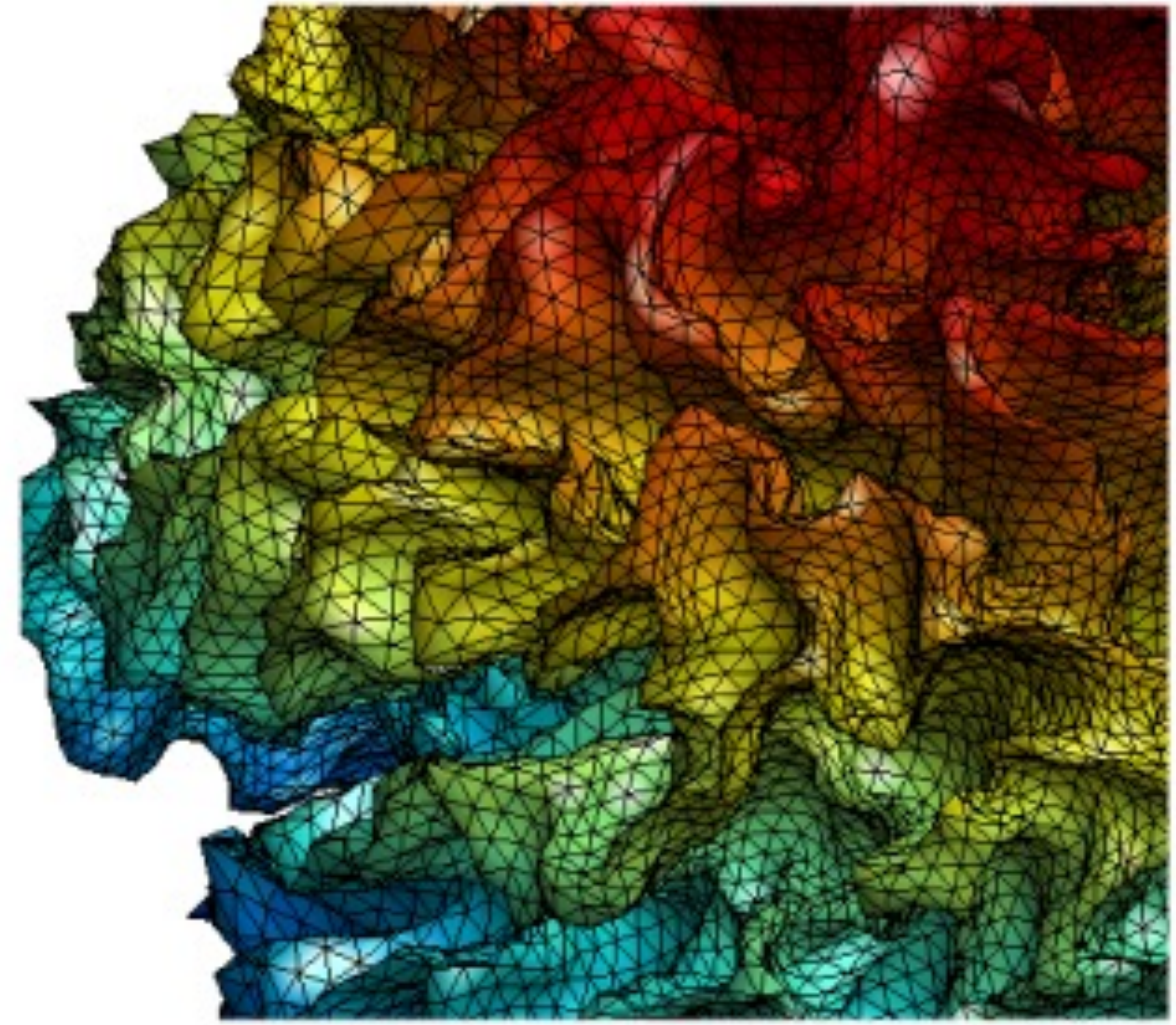
Euler characteristic:

$$\chi = \beta_0 - \beta_1 = 2$$



$$\beta_0 = 1, \beta_1 = 2, \beta_2 = 1$$

(1,2,1,0,0,…)

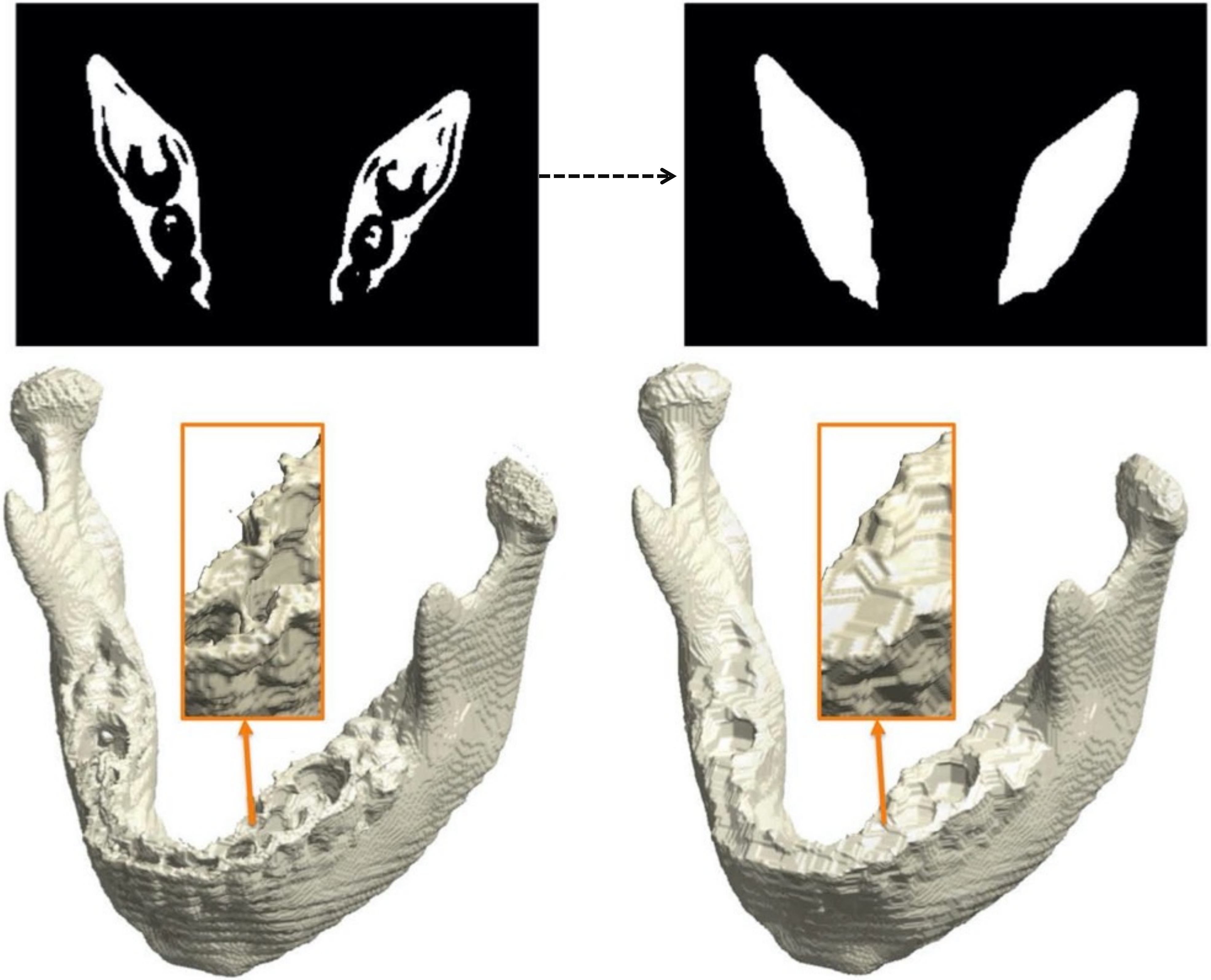
 

Euler characteristic of a surface mesh from SurfStat

$N - E + F = 2$ for a surface topologically equivalent to a sphere. For each triangle, there are three edges. Since two adjacent triangles share the same edge, the total number of edges is $E = 3F/2 \rightarrow F = 2N - 4$ for a closed surface.

Can be used to correct topological artifacts in FreeSurfer

Topology correction in CT segmentation



Hole & handles corrected using Euler characteristic

<u>*Chung et al. 2015 Medical Image Analysis.* 22:63-76</u>

Keith Worsley's random field theory

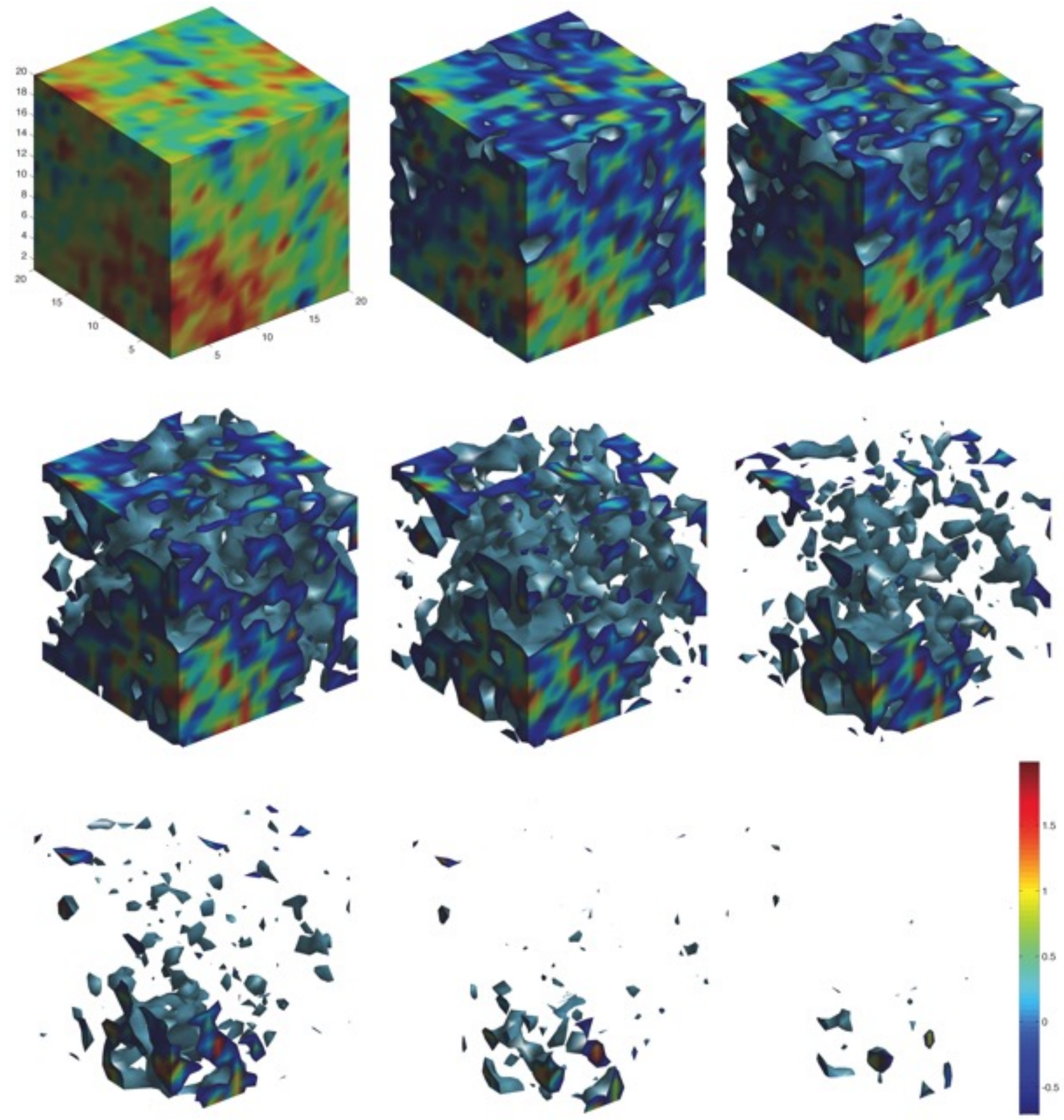
Random field

$$P\Big(\sup_{x\in\mathbb{M}} T(x) > h\Big)$$

$$A_h = \{x \in \mathbb{M} : T(x) > h\}$$

$$P\Big(\sup_{x\in\mathbb{M}} T(x) > h\Big) = \mathbb{E}\chi(A_h)$$

$$\chi(A_h) = \sum_j (-1)^j \beta_j(A_h)$$



Milor 1963 Morse theory

Adler, 1994 The geometry of random fields

Worsley et al., 1996 Human Brain Mapping

Morse Filtration

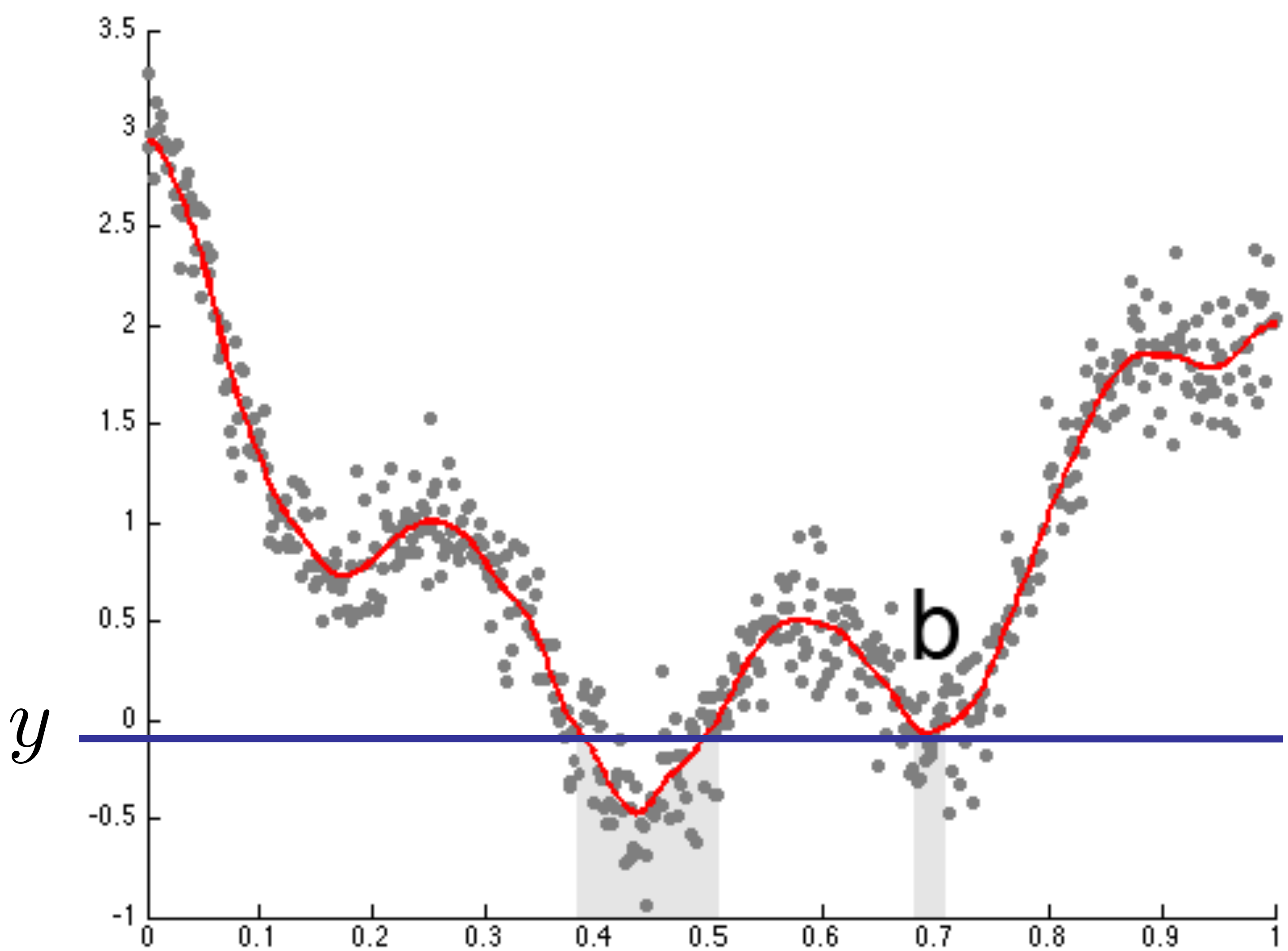
Chung et al., 2009 Information Processing in Medical Imaging (IPMI) 5636:386-397.

`PH_morse1D.m`

Morse theory for functional data

$$Y(t) = \mu(t) + \epsilon(t)$$

Unknown signal μ is assumed to be a Morse function: all critical values are unique.



Sublevel set

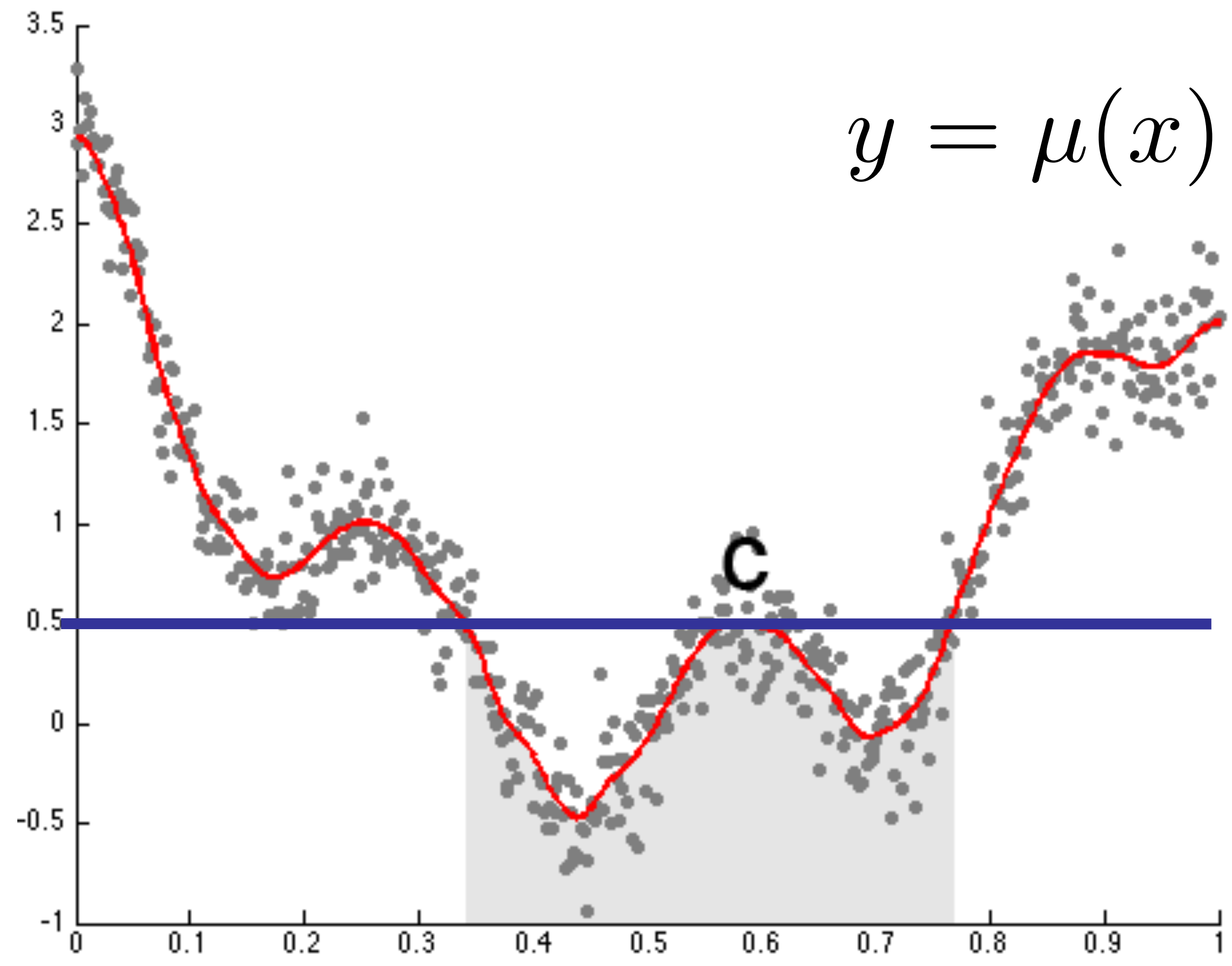
$$R_y = \{t : \mu(t) \leq y\}$$

The topology of sublevel set is characterized by Betti-0 number only

Morse filtration

Sublevel set

$$R_y = \{t : \mu(t) \leq y\}$$



Morse filtration

$$R_b \subset R_c$$

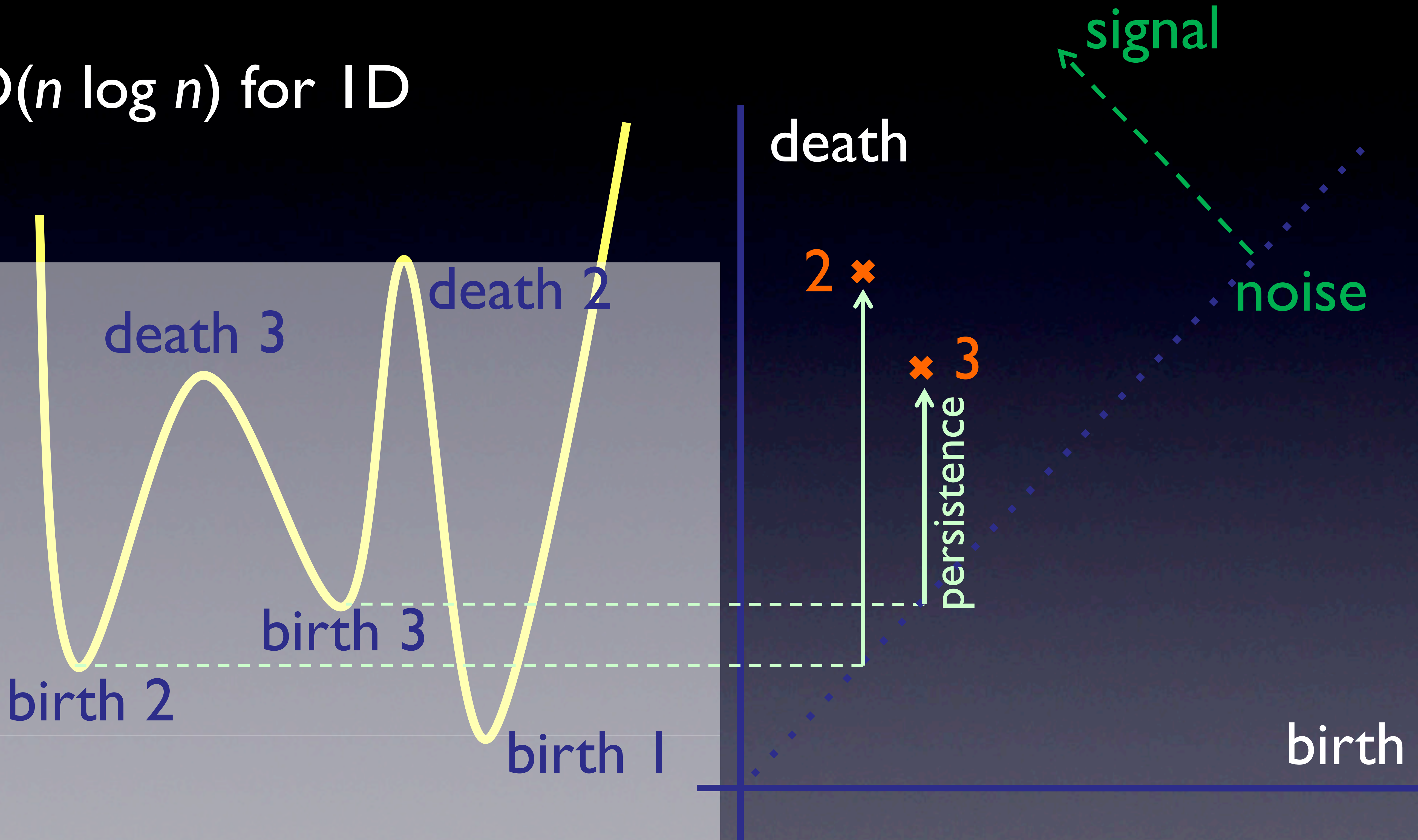
Component dies at c

$$\beta_0(R_c) = \beta_0(R_b) - 1$$

PH_morse1D.m

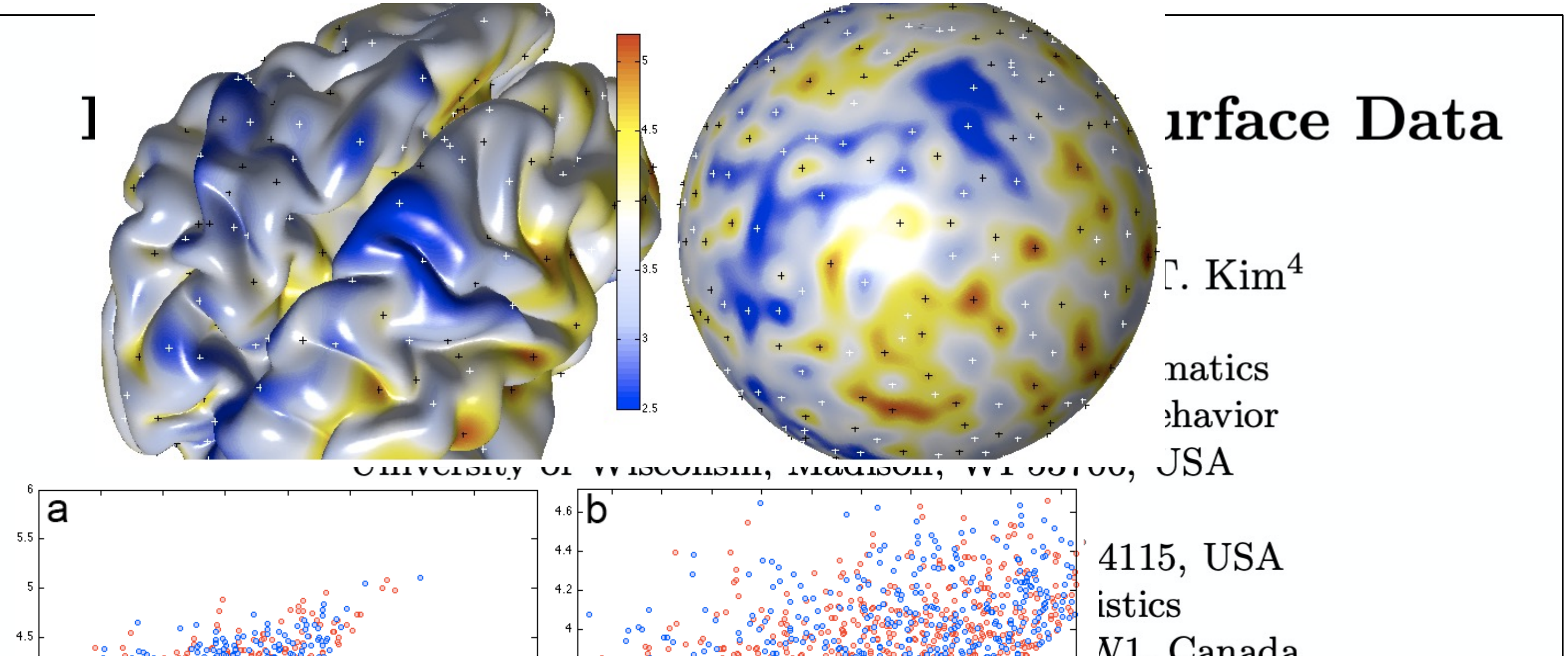
Persistence Diagram (PD)

O(n log n) for 1D



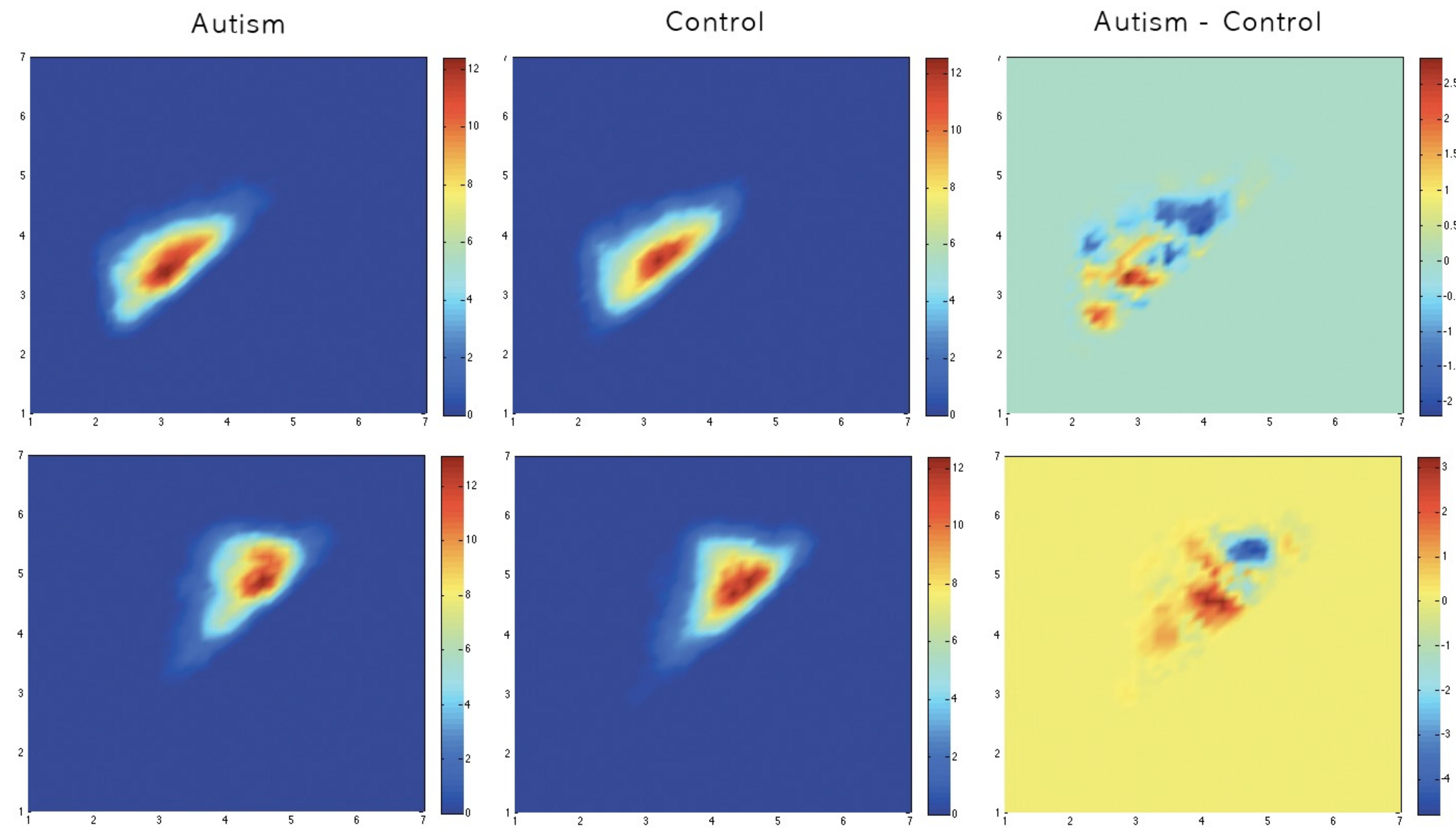
Elder's rule:

Pair the time of death with the time of the closest earlier birth.



Chung et al., 2009

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



First TDA paper in medical imaging

Boundary matrix

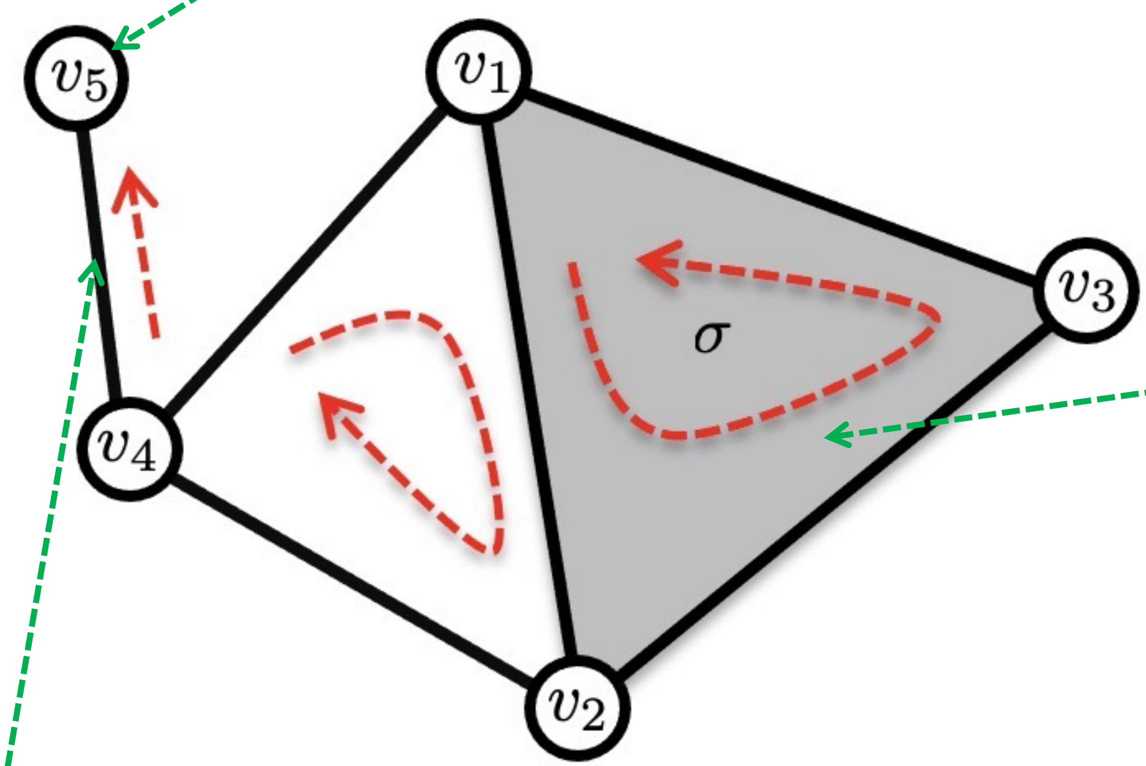
n-simplex

The basic building block of persistent homology

The smallest convex set containing *n+1* points

$$\sum_{i=0}^{n} x_i = 1, x_i \geq 0$$

0-simplex $[v_5]$



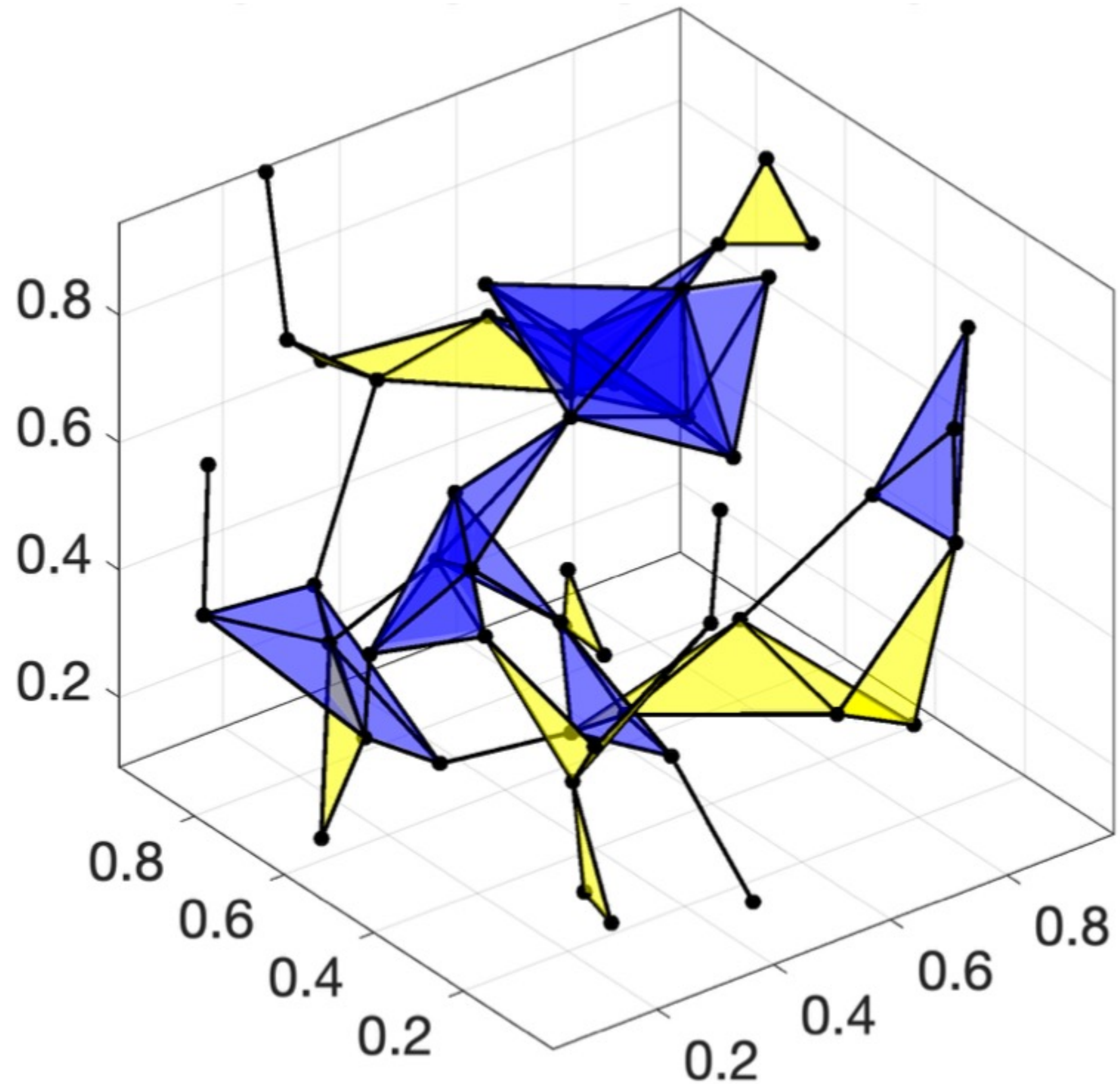
2-simplex

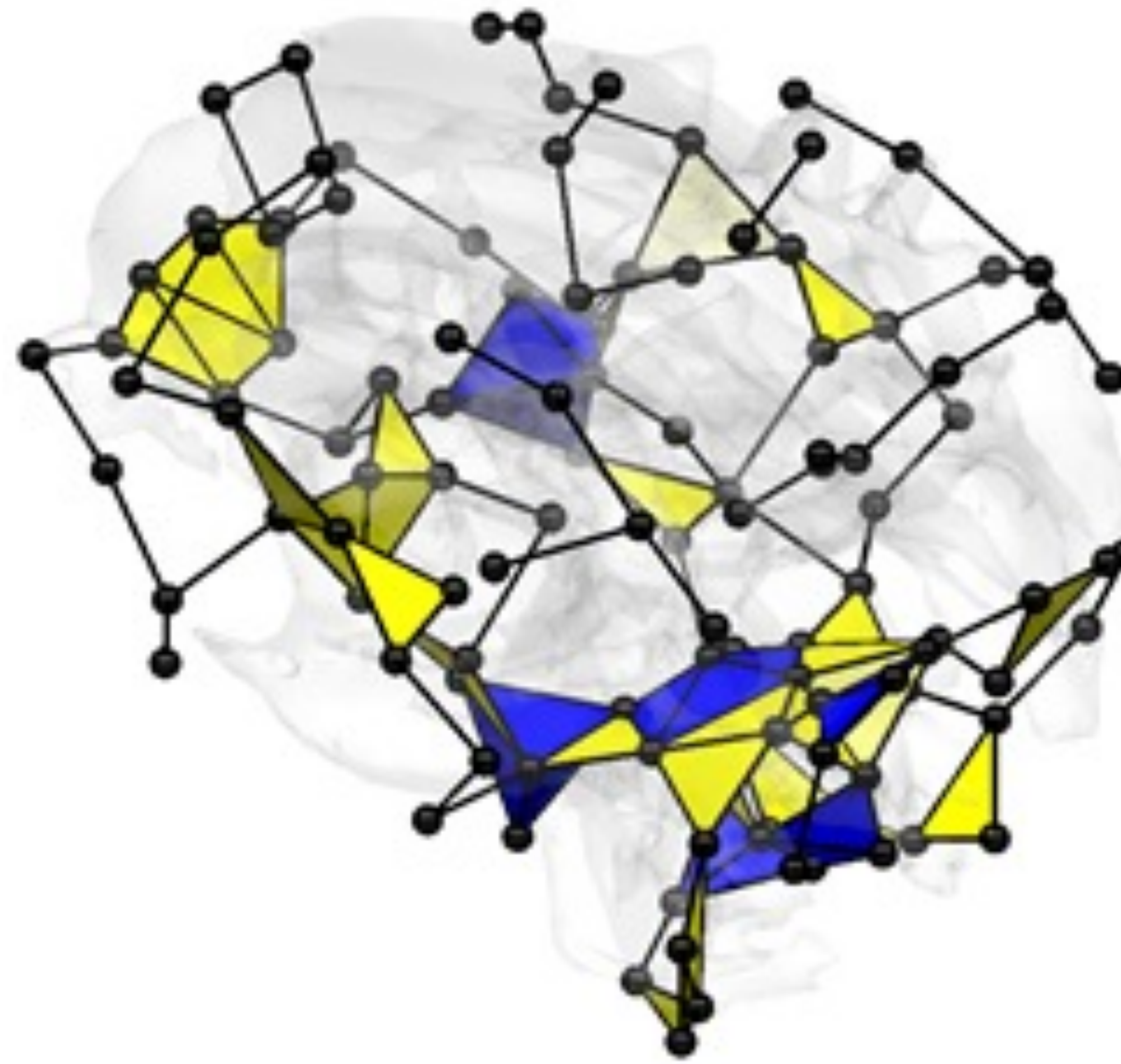
$$\sigma = [v_1, v_2, v_3]$$

1-simplex $[v_4, v_5] = -[v_5, v_4]$

Simplicial complex

A simplicial complex is a set composed of points, line segments, triangles, and their n-dimensional counterparts.



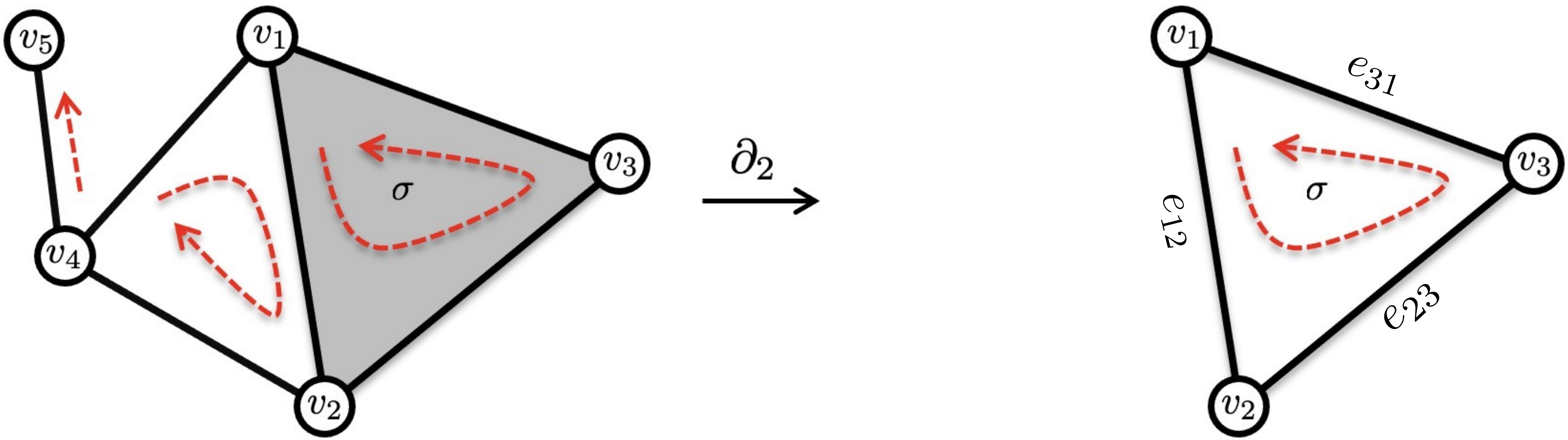


PH_rips.m

Boundary operators ∂_k

∂_k Removes the filled-in interior of *k*-simplexes

$$\partial_k : C_k \rightarrow C_{k-1}$$

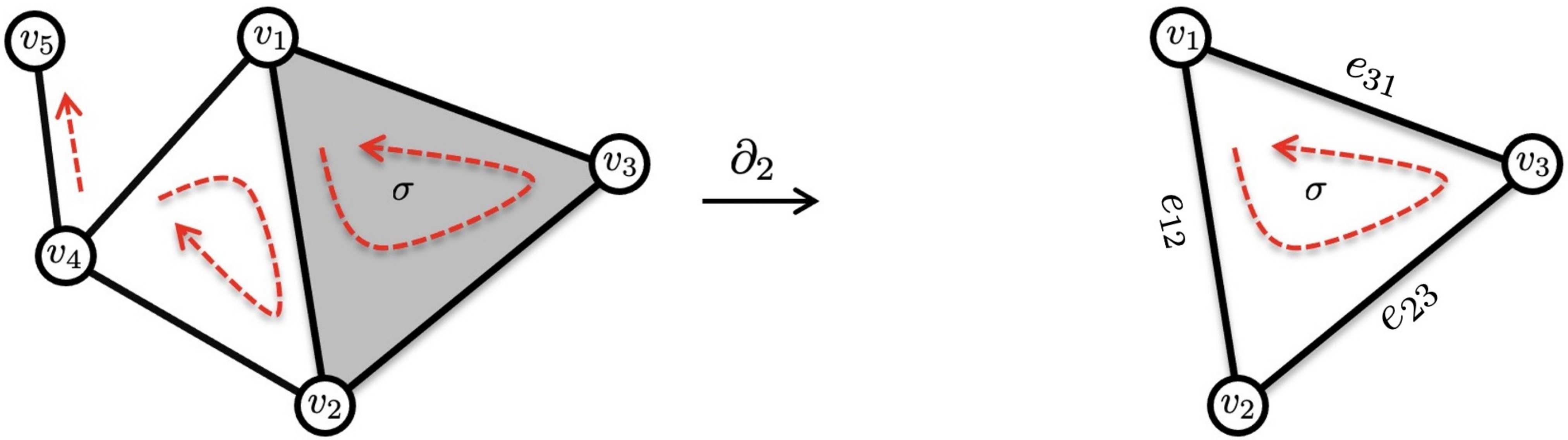


$$\partial_2 \sigma = [v_1, v_2] + [v_2, v_3] + [v_3, v_1]$$

$$\partial_1 \partial_2 \sigma = v_2 - v_1 + v_3 - v_2 + v_1 - v_3 = 0$$

Node to edge connectivity information

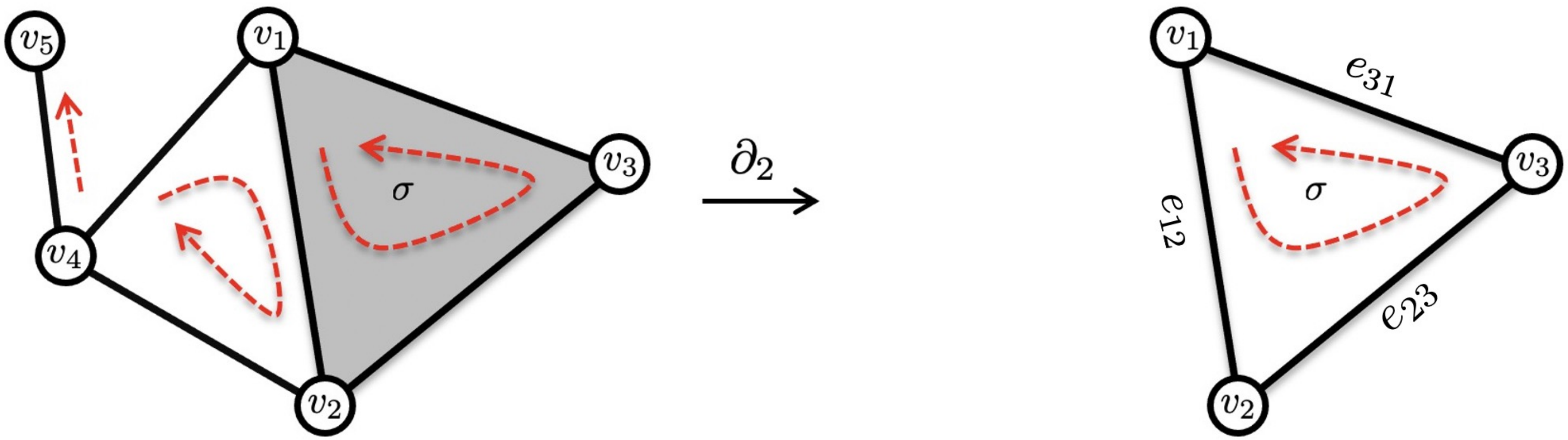
Boundary matrix ∂_0



$$\boldsymbol{\partial}_0 = \begin{array}{cc} & \begin{array}{ccccc} v_1 & v_2 & v_3 & v_4 & v_5 \end{array} \\ 0 & \begin{pmatrix} 0 & 0 & 0 & 0 & 0 \end{pmatrix} \end{array}$$

PH_boundary.m

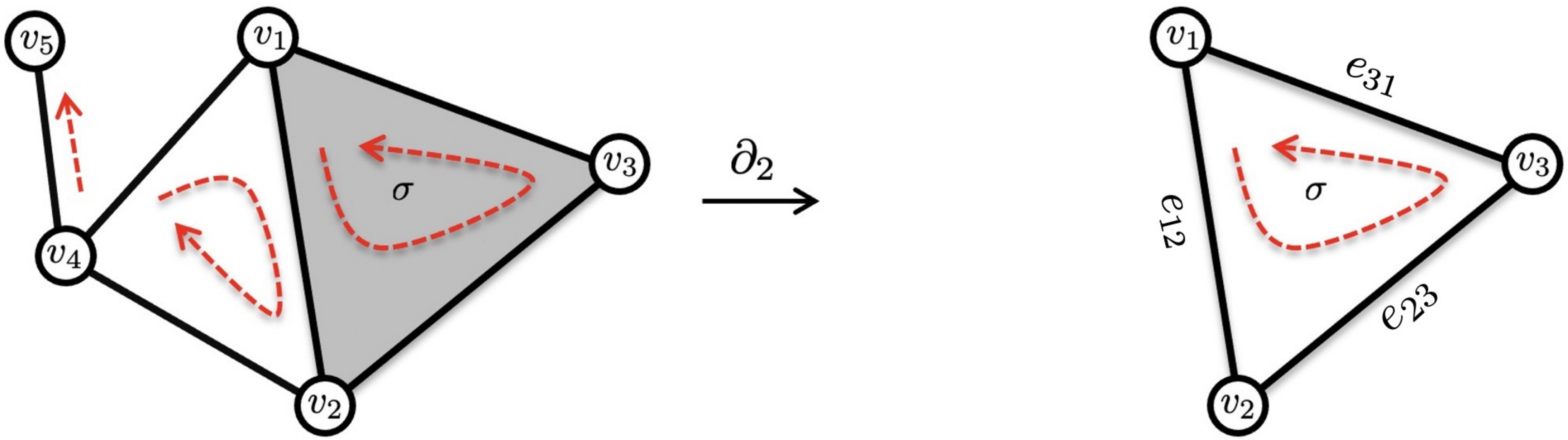
Boundary matrix ∂_1 edge to node



$$\partial_1 \partial_2 \sigma = v_2 - v_1 + v_3 - v_2 + v_1 - v_3 = 0$$

$$\boldsymbol{\partial}_1 = \begin{array}{c} \\ v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \end{array} \begin{array}{c} \begin{array}{cccccc} e_{12} & e_{23} & e_{31} & e_{24} & e_{41} & e_{45} \end{array} \\ \begin{pmatrix} -1 & 0 & 1 & 0 & 1 & 0 \\ 1 & -1 & 0 & -1 & 0 & 0 \\ 0 & 1 & -1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & -1 & -1 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix} \end{array}$$

Boundary matrix ∂_2 face to edge



$$\partial_2\sigma = [v_1, v_2] + [v_2, v_3] + [v_3, v_1]$$

$$\boldsymbol{\partial}_2 = \begin{array}{c c} & \sigma \\ \begin{array}{c} e_{12} \\ e_{23} \\ e_{31} \\ e_{24} \\ e_{41} \\ e_{45} \end{array} & \begin{pmatrix} 1 \\ 1 \\ 1 \\ 0 \\ 0 \\ 0 \end{pmatrix} \end{array}$$

PH_boundary.m

Boundary matrix ∂_k

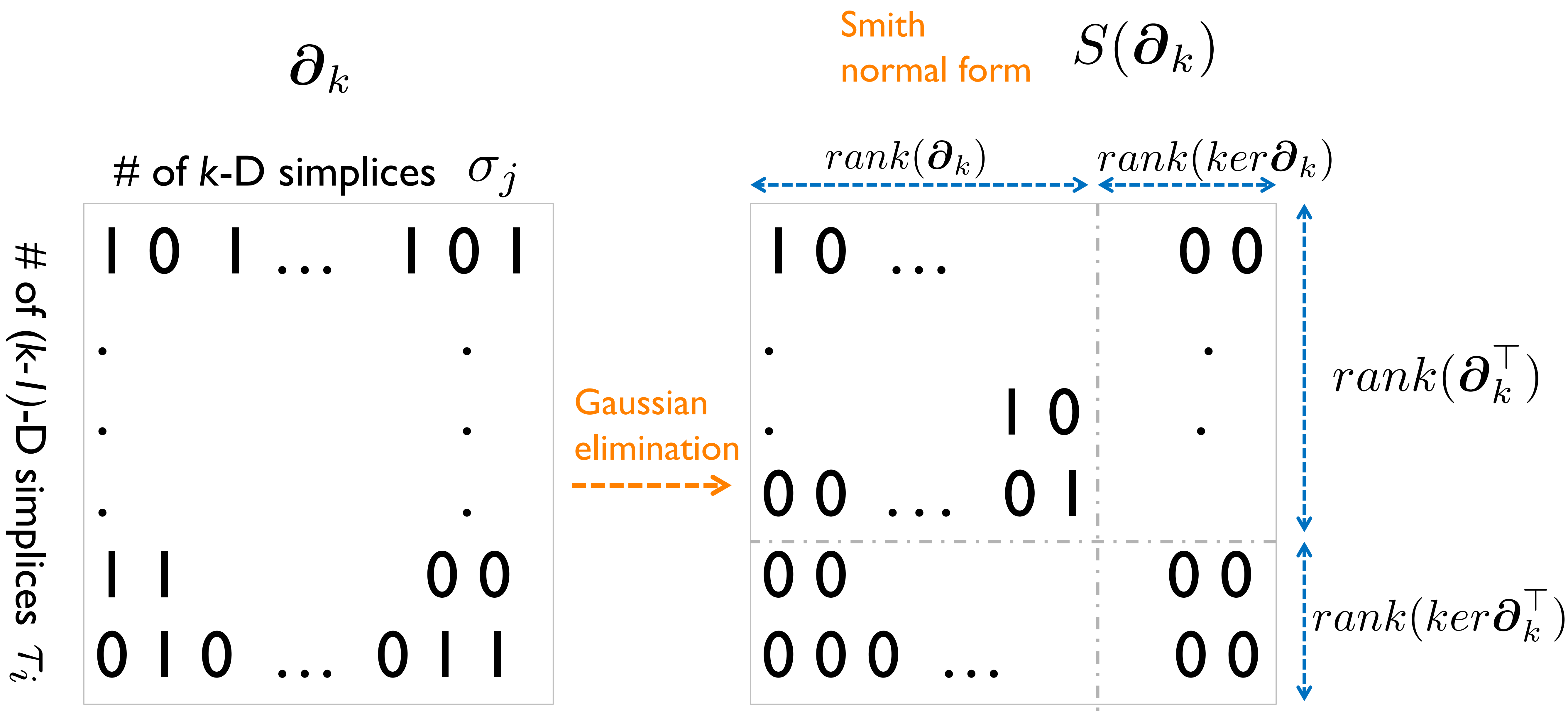
(*i*,*j*)-th entry = 1 if $\tau_i \subset \sigma_j$

Sign depends on the orientation of τ_i

$$
\begin{array}{c|c}
 & \text{\# of } k\text{-dimensional simplices } \sigma_j \\
\hline
\text{\# of } (k\text{-}1)\text{-dimensional simplices } \tau_i &
\begin{bmatrix}
1 & 0 & 1 & \ldots & 1 & 0 & 1 \\
\cdot & & & & \cdot & & \\
\cdot & & & & \cdot & & \\
\cdot & & & & \cdot & & \\
1 & 1 & & & & 0 & 0 \\
0 & 1 & 0 & \ldots & 0 & 1 & -1
\end{bmatrix}_{\partial_k}
\end{array}
$$

PH_boundary.m

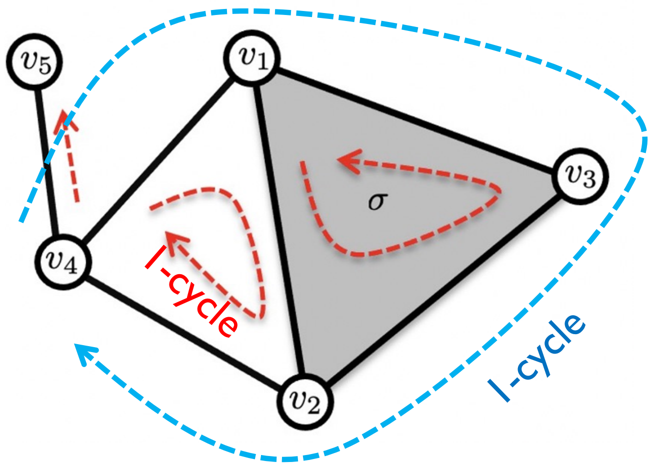
Rank nullity theorem for boundary matrix



$$\beta_k = rank(ker\boldsymbol{\partial}_k) - rank(\boldsymbol{\partial}_{k+1})$$

PH_boundary_betti.m

Computing Betti numbers through boundary matrices



$$\mathcal{S}(\boldsymbol{\partial}_1) = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}, \quad \mathcal{S}(\boldsymbol{\partial}_2) = \begin{pmatrix} 1 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

$$\beta_0 = rank(ker\boldsymbol{\partial}_0) - rank(\boldsymbol{\partial}_1)$$ = 5-4

$$\beta_1 = rank(ker\boldsymbol{\partial}_1) - rank(\boldsymbol{\partial}_2)$$ = 2-1

PH_boundary_betti.m

k-th Hodge Laplacian

PH_hodge.m

$$\Delta_k = \partial_{k+1}\partial_{k+1}^\top + \partial_k^\top \partial_k$$

0th Hodge Laplacian

Graph Laplacian

# of nodes

$$\Delta_0 = \boxed{\partial_1\partial_1^\top}$$

# of nodes

1st Hodge Laplacian

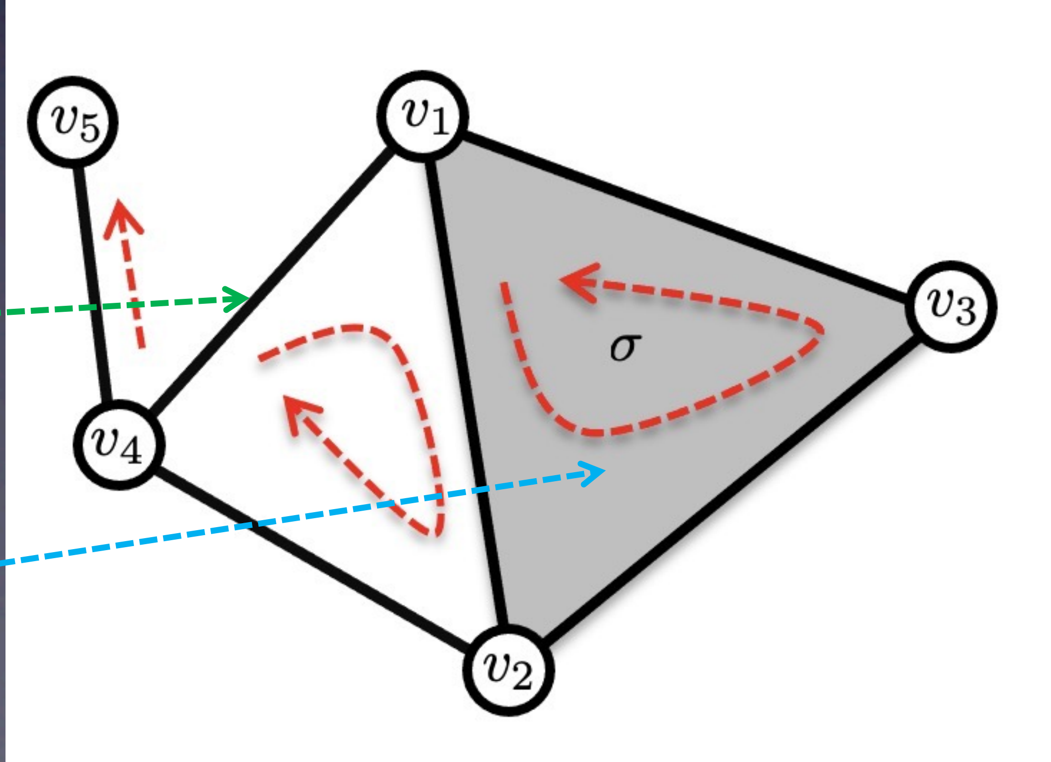
# of edges

# of edges

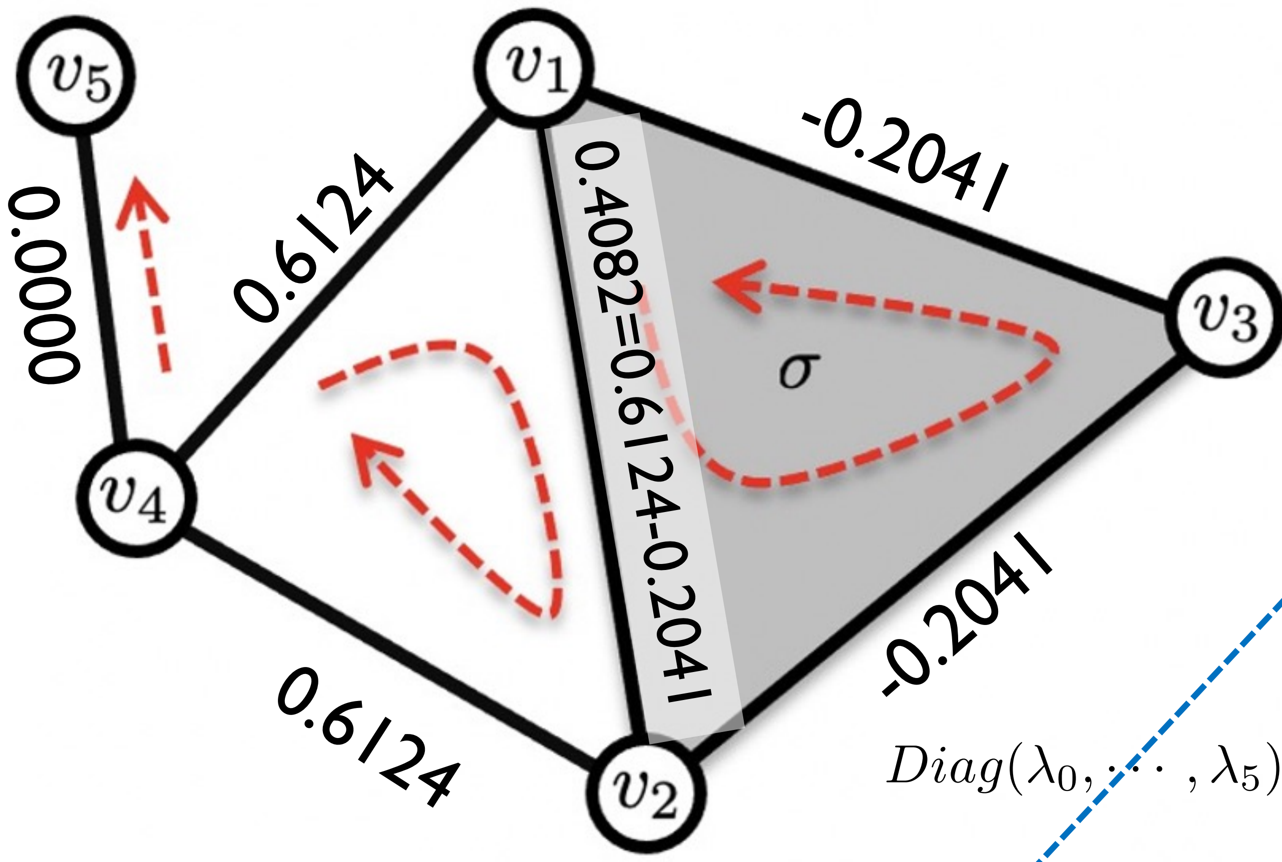
$$\Delta_1 = \boxed{\partial_2\partial_2^\top} + \boxed{\partial_1^\top\partial_1}$$

# of edges

# of edges



Eigenvectors of Hodge Laplacian



$$\Delta_1 = \boldsymbol{\partial}_2\boldsymbol{\partial}_2^\top + \boldsymbol{\partial}_1^\top\boldsymbol{\partial}_1$$

$$ker\Delta_1$$

span

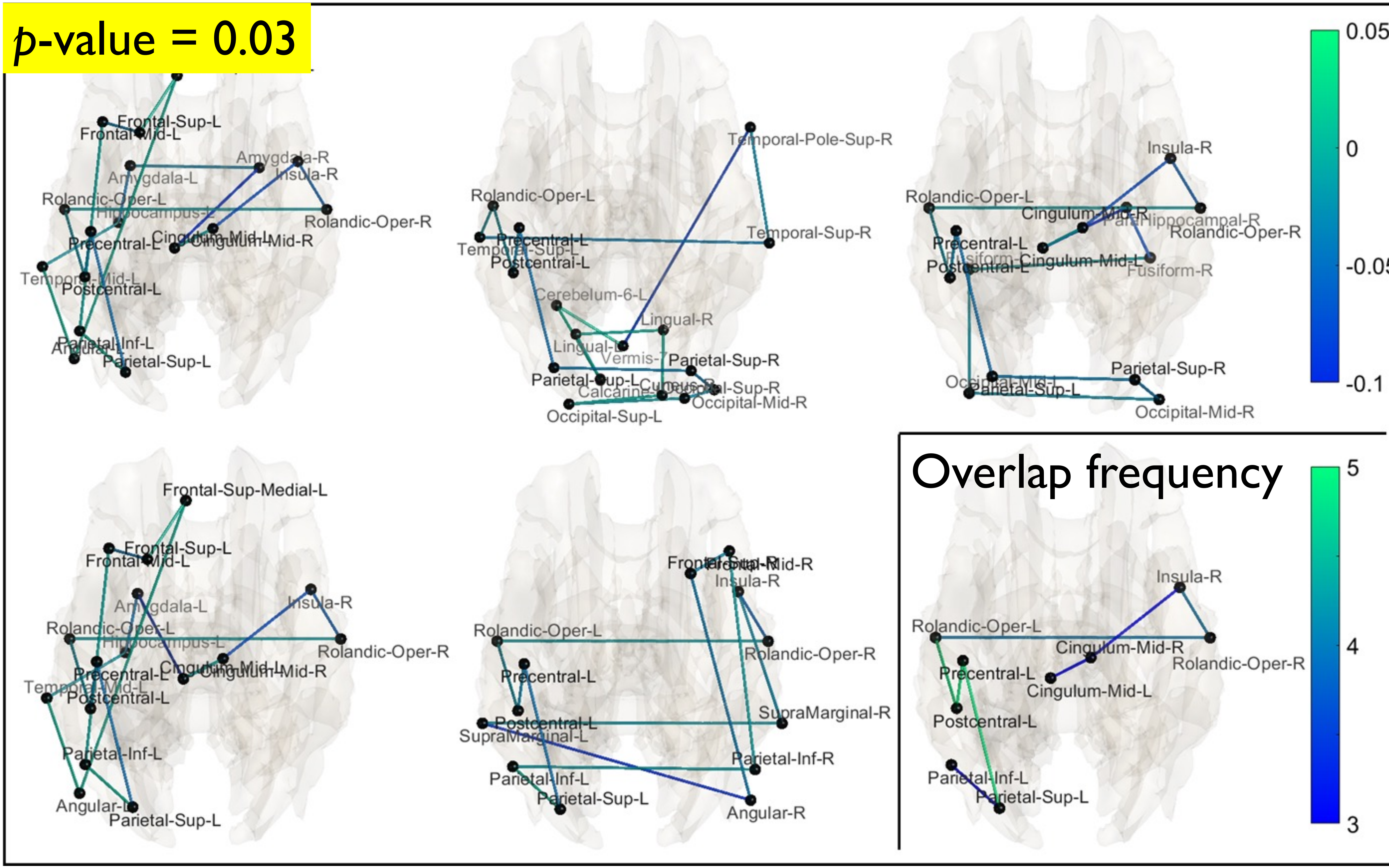
$$Diag(\lambda_0, \cdots, \lambda_5) = \begin{pmatrix} \boxed{0.0000} & 0 & 0 & 0 & 0 & 0 \\ 0 & 0.8299 & 0 & 0 & 0 & 0 \\ 0 & 0 & 2.6889 & 0 & 0 & 0 \\ 0 & 0 & 0 & 3.0000 & 0 & 0 \\ 0 & 0 & 0 & 0 & 4.0000 & 0 \\ 0 & 0 & 0 & 0 & 0 & 4.4812 \end{pmatrix}$$

$$(\mathbf{f}_0, \cdots, \mathbf{f}_5) = \begin{pmatrix} 0.4082 & -0.0000 & 0.0000 & 0.5774 & 0.7071 & -0.0000 \\ -0.2041 & 0.1993 & -0.5765 & 0.5774 & -0.3536 & 0.3578 \\ -0.2041 & -0.1993 & 0.5765 & 0.5774 & -0.3536 & -0.3578 \\ 0.6124 & -0.4325 & 0.1793 & -0.0000 & -0.3536 & 0.5299 \\ 0.6124 & 0.4325 & -0.1793 & -0.0000 & -0.3536 & -0.5299 \\ 0.0000 & -0.7392 & -0.5207 & 0.0000 & 0.0000 & -0.4271 \end{pmatrix}$$

Basis vector for cycles

Five biggest cycle differences (male – female) in HCP

p-value = 0.03

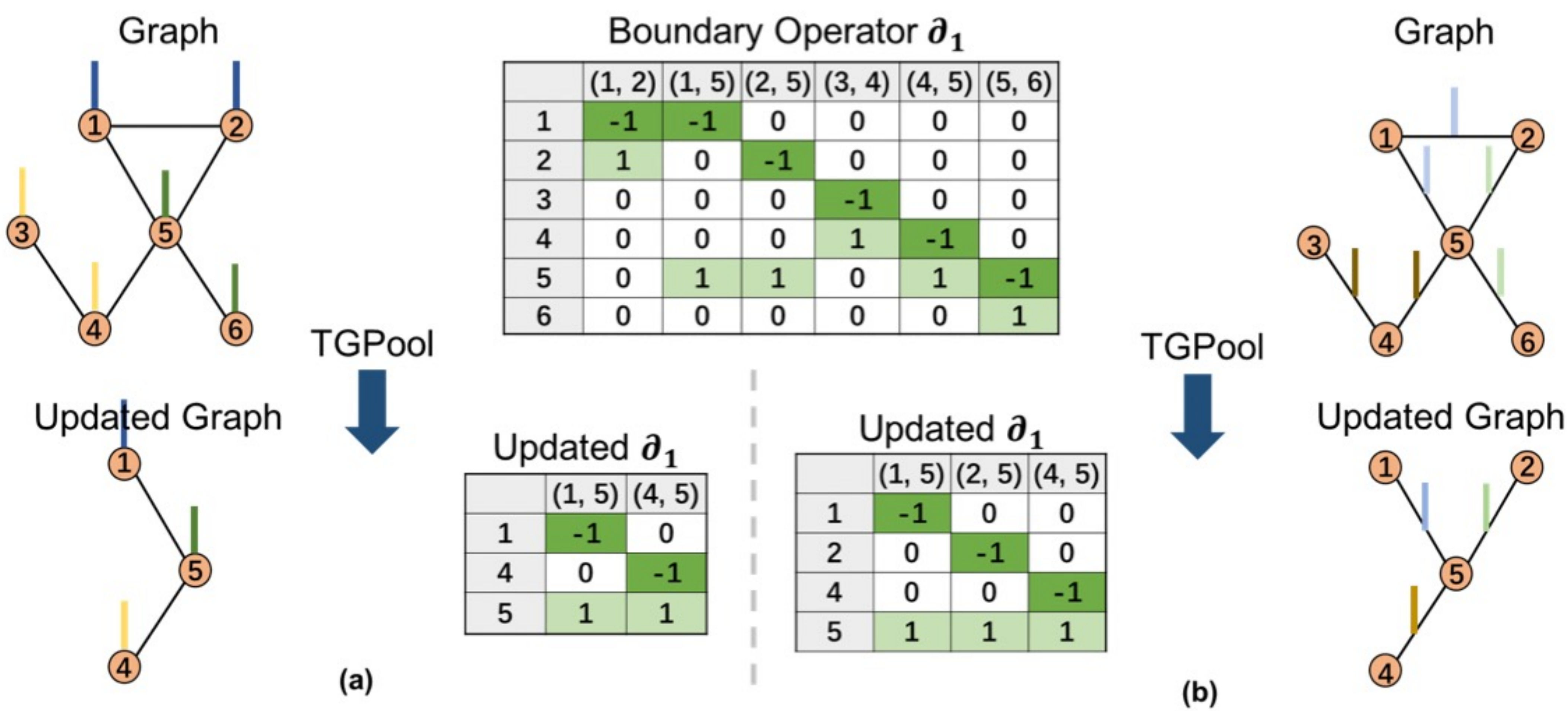


Anand et al. 2023, IEEE TMI in press arXiv:2110.14599

Spectral convolution on graphs using Hodge Laplacian

$$f'(\cdot) = h * f(\cdot) = \sum_{p=0}^{P-1} \theta_p T_p(\boldsymbol{\mathcal{L}}_k) f(\cdot)$$

Topological pooling



Boundary Operator ∂_1

	(1, 2)	(1, 5)	(2, 5)	(3, 4)	(4, 5)	(5, 6)
1	-1	-1	0	0	0	0
2	1	0	-1	0	0	0
3	0	0	0	-1	0	0
4	0	0	0	1	-1	0
5	0	1	1	0	1	-1
6	0	0	0	0	0	1

Updated ∂_1 (a)

	(1, 5)	(4, 5)
1	-1	0
4	0	-1
5	1	1

Updated ∂_1 (b)

	(1, 5)	(2, 5)	(4, 5)
1	-1	0	0
2	0	-1	0
4	0	0	-1
5	1	1	1

Huang et al. 2023 IPMI oral, in press, arxiv:2302.09323

Rips filtrations

Rips filtration

PH_rips.m

Metric space

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

Node set

Metric

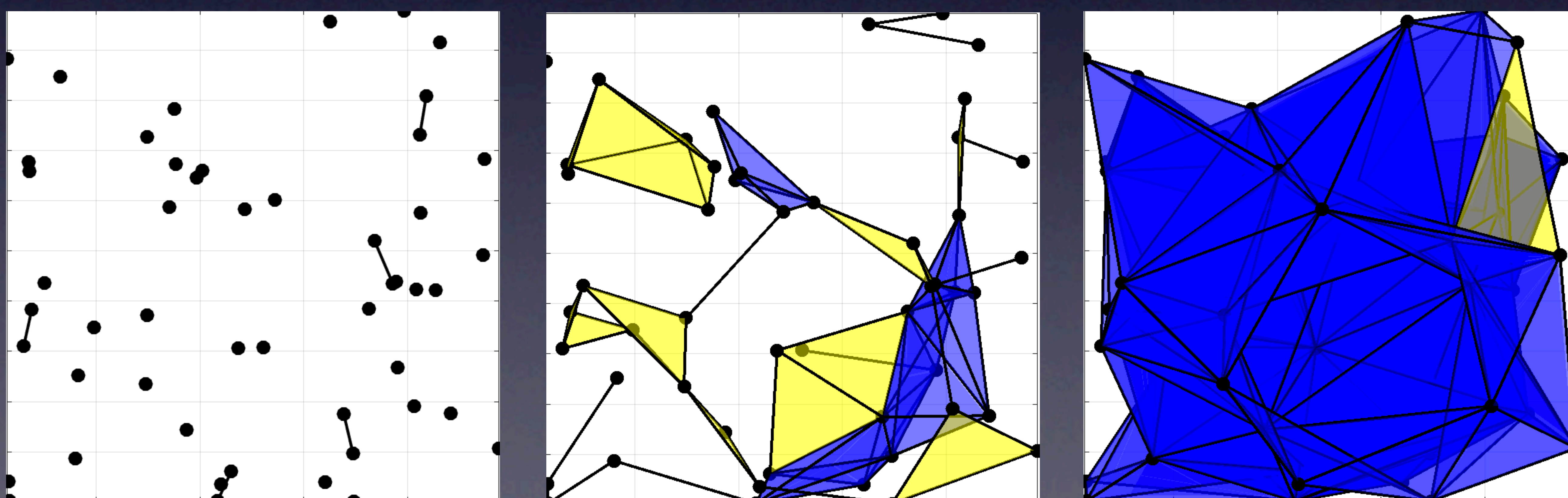
$$w_{ik} < w_{ij} + w_{jk}$$

Rips filtration

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

for filtration values

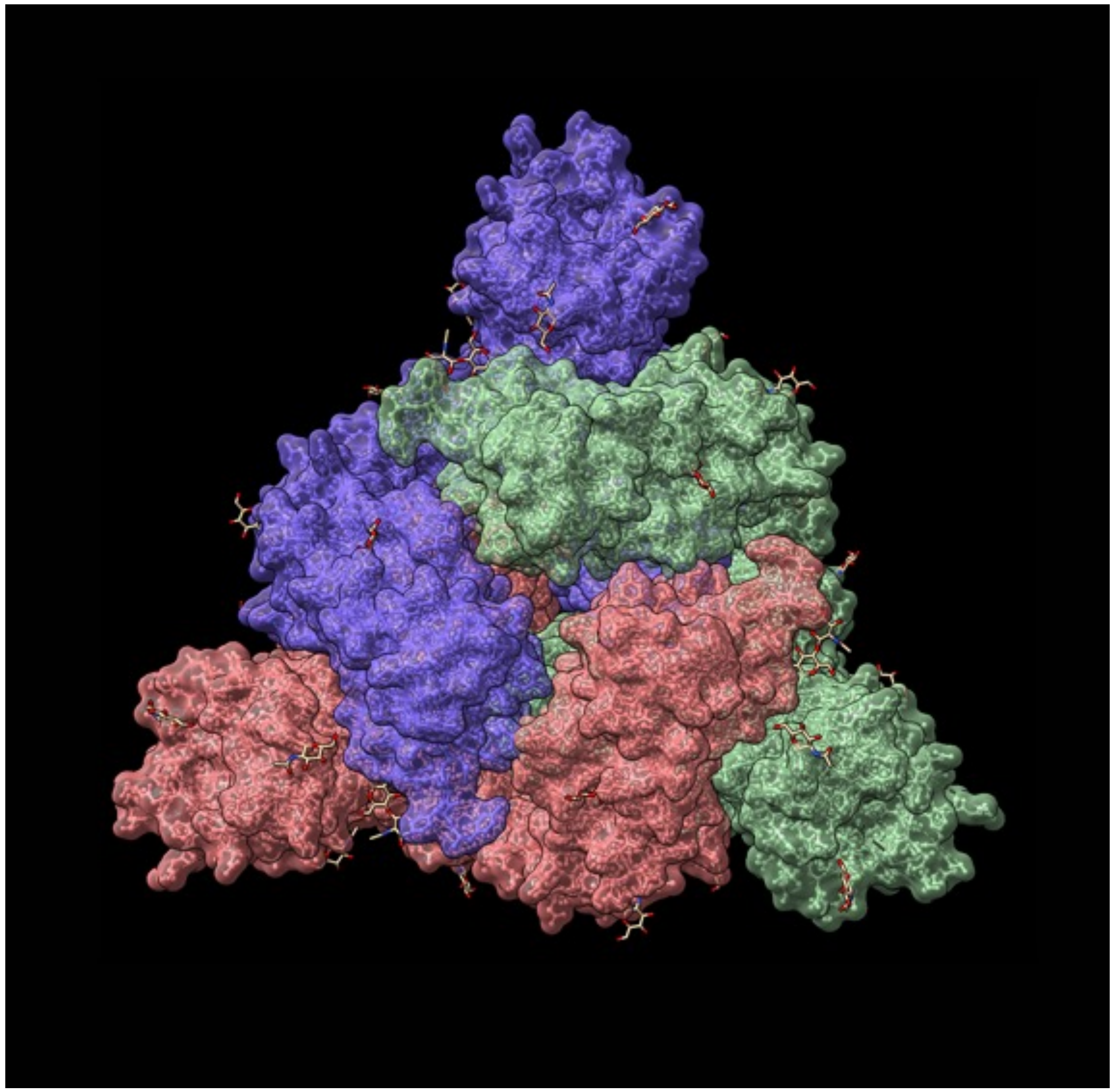
$$\epsilon_0 < \epsilon_1 < \epsilon_2 < \cdots$$

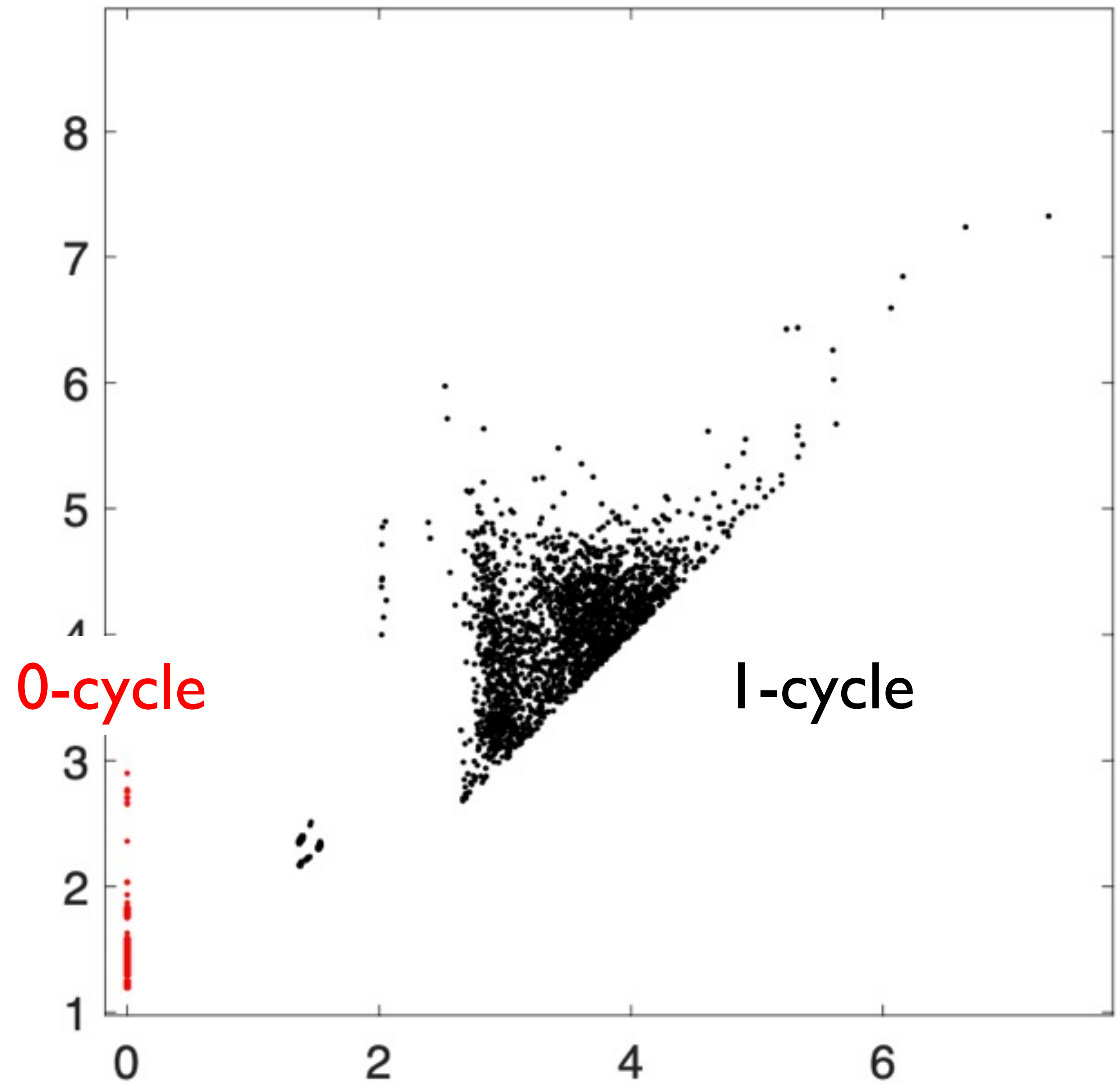


$\epsilon = 0.1$ $\epsilon = 0.3$ $\epsilon = 0.5$

Persistence Diagram (PD) of a protein molecule

Rips filtration on distance between 8000 atoms

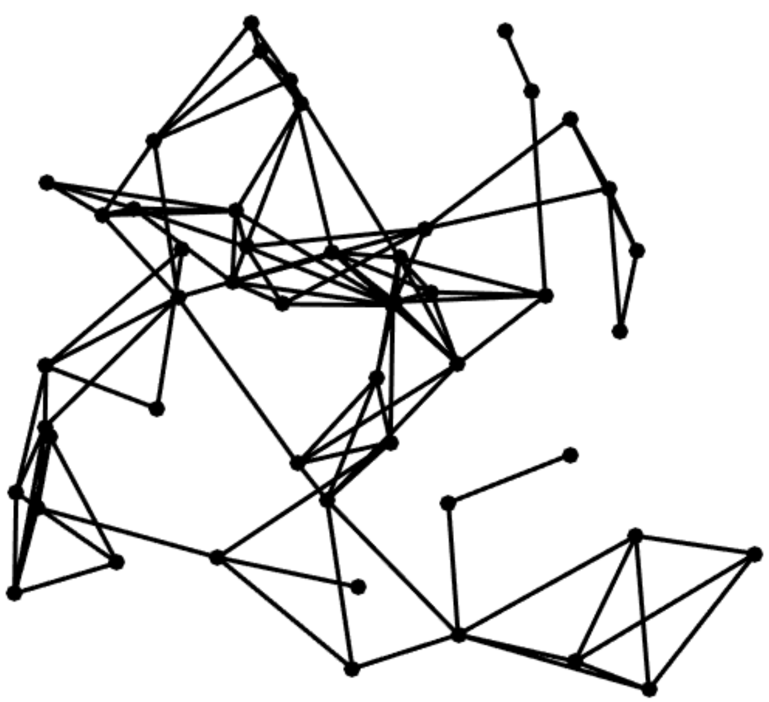




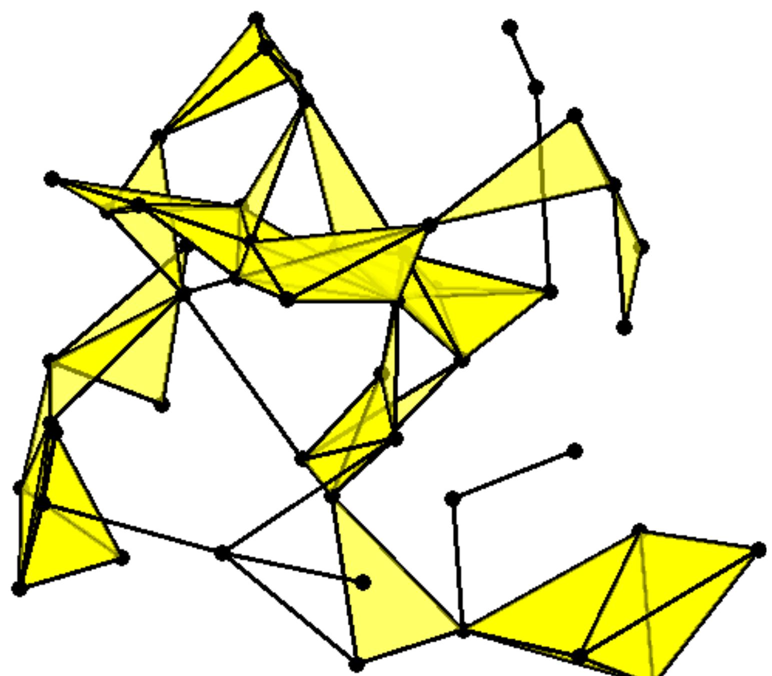
Extremely slow computation → Simply use graph filtration

k-skeleton

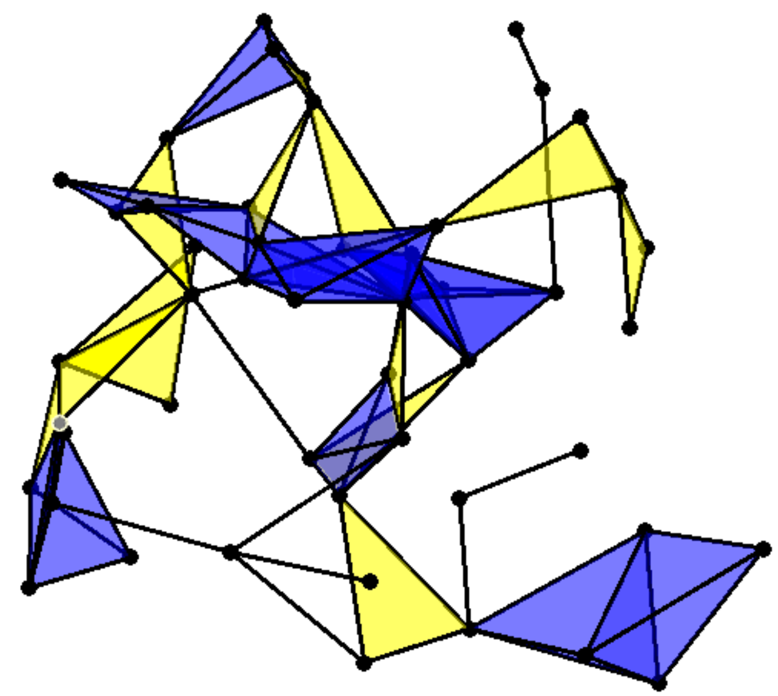
A simplicial complex consisting of up to k-simplices



1-skeleton



2-skeleton



3-skeleton

PH_rips.m

Graph filtrations

Baseline filtration for brain networks introduced in

Lee et al. 2011 ISBI
Lee et al. 2011 MICCAI 302-309
Lee et al. 2012 IEEE Transactions on Medical Imaging 31:2267-2277

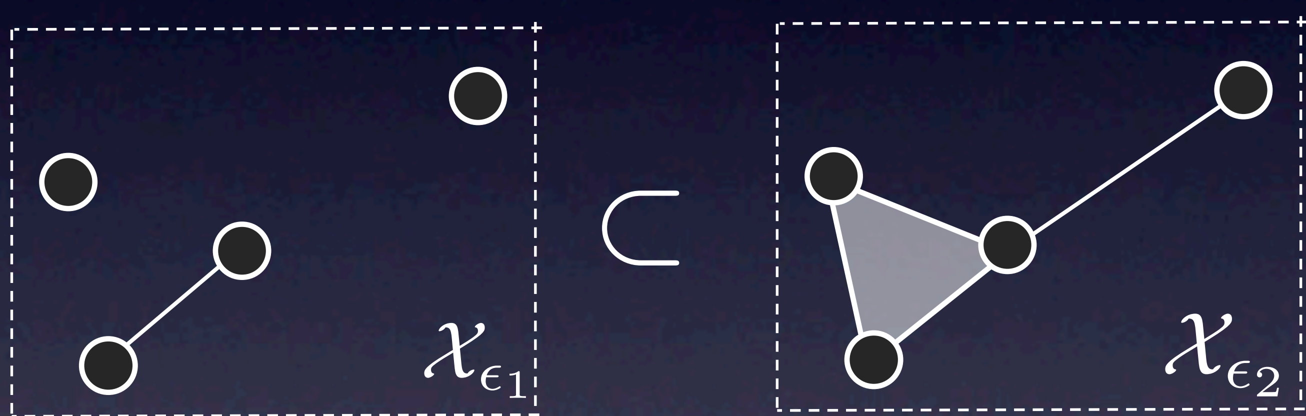
Rips filtration vs. graph filtration

Metric space

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

Node set Metric

Rips complex = Simplicial complex



Rips filtration

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

for increased radius

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

PH_rips.m

Weighted graph

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

Node set Edge weight

Binary graph: 1-skeleton

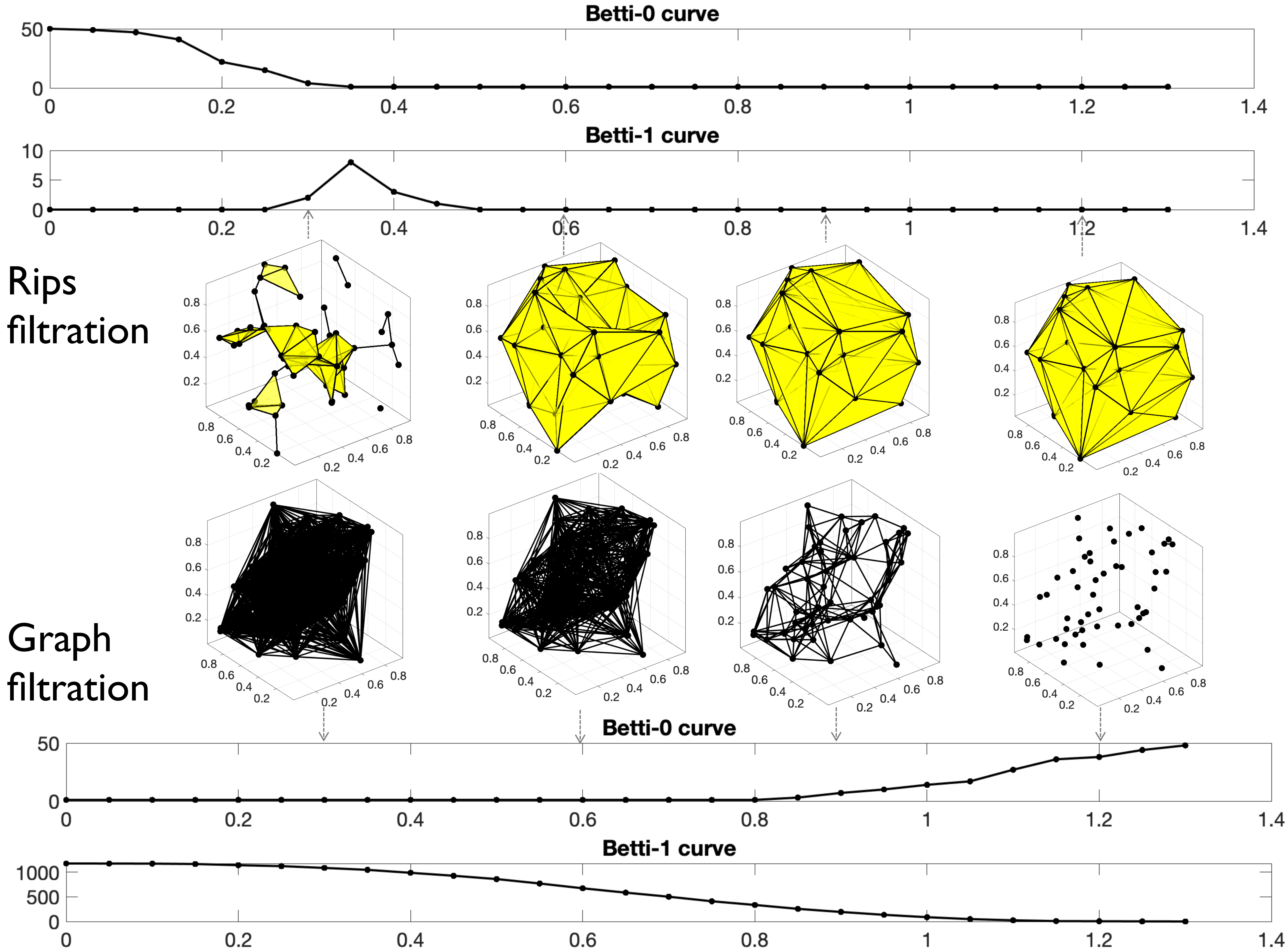
Graph filtration

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

for increased edge weights

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

PH_graph.m



Betti-0 curve
Betti-1 curve
Rips filtration
Graph filtration
Betti-0 curve
Betti-1 curve

How to compute the number of cycles in big network data?

How many cycles in the network?

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

Fast computation of Betti curves

Computation of β_0: Can use a built-in function in MATLAB.

```
[beta_0, S] = graphconncomp(adj)
```

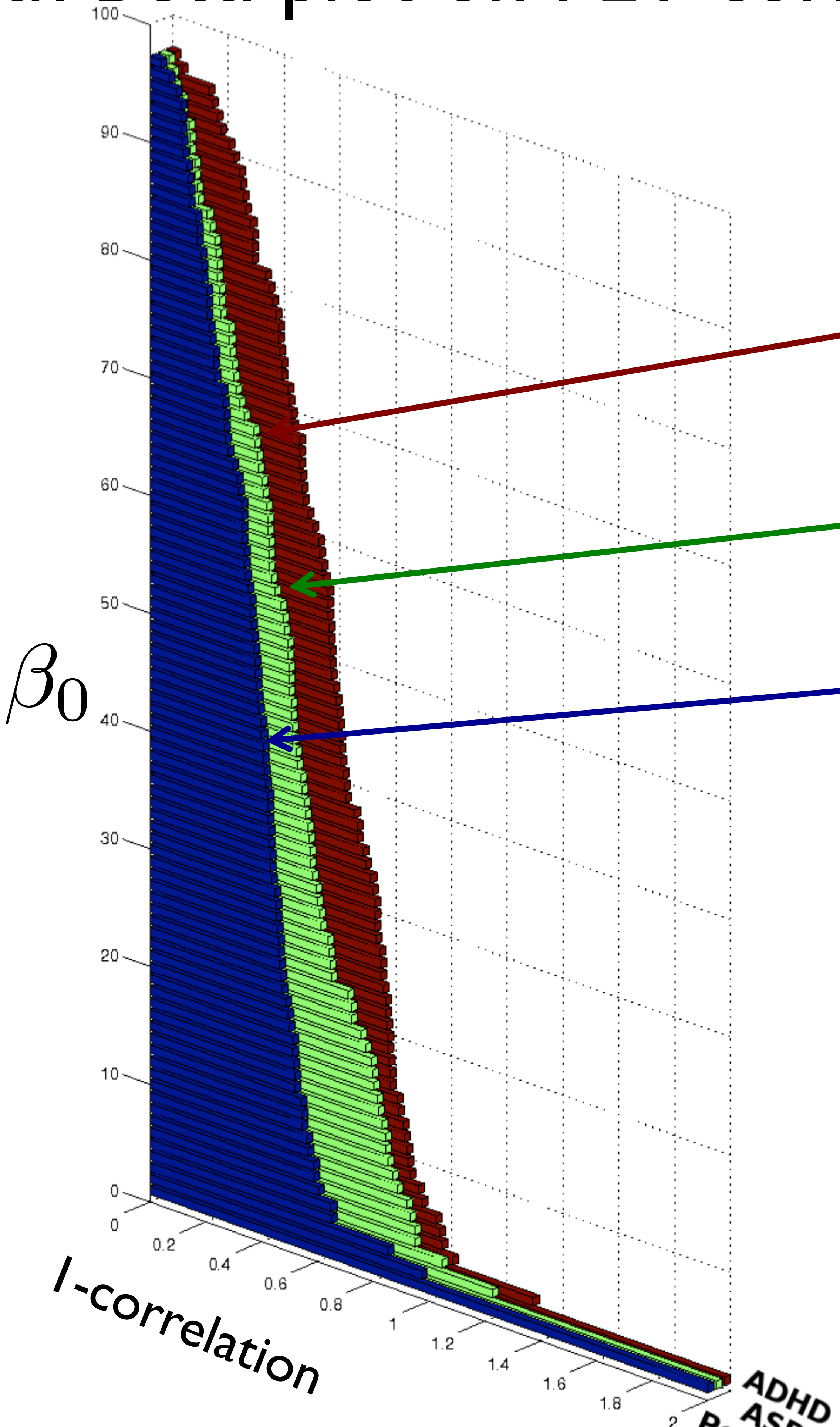
Computation of β_1: As a function of β_0

$$\beta_1 = \beta_0 - p + q$$

```
q=sum(sum(adj))/2;
beta_1 = beta_0 - p + q;
```

PH_betti.m

0-th Betti plot on PET correlation network



24 attention deficit hyperactivity disorder (ADHD) children

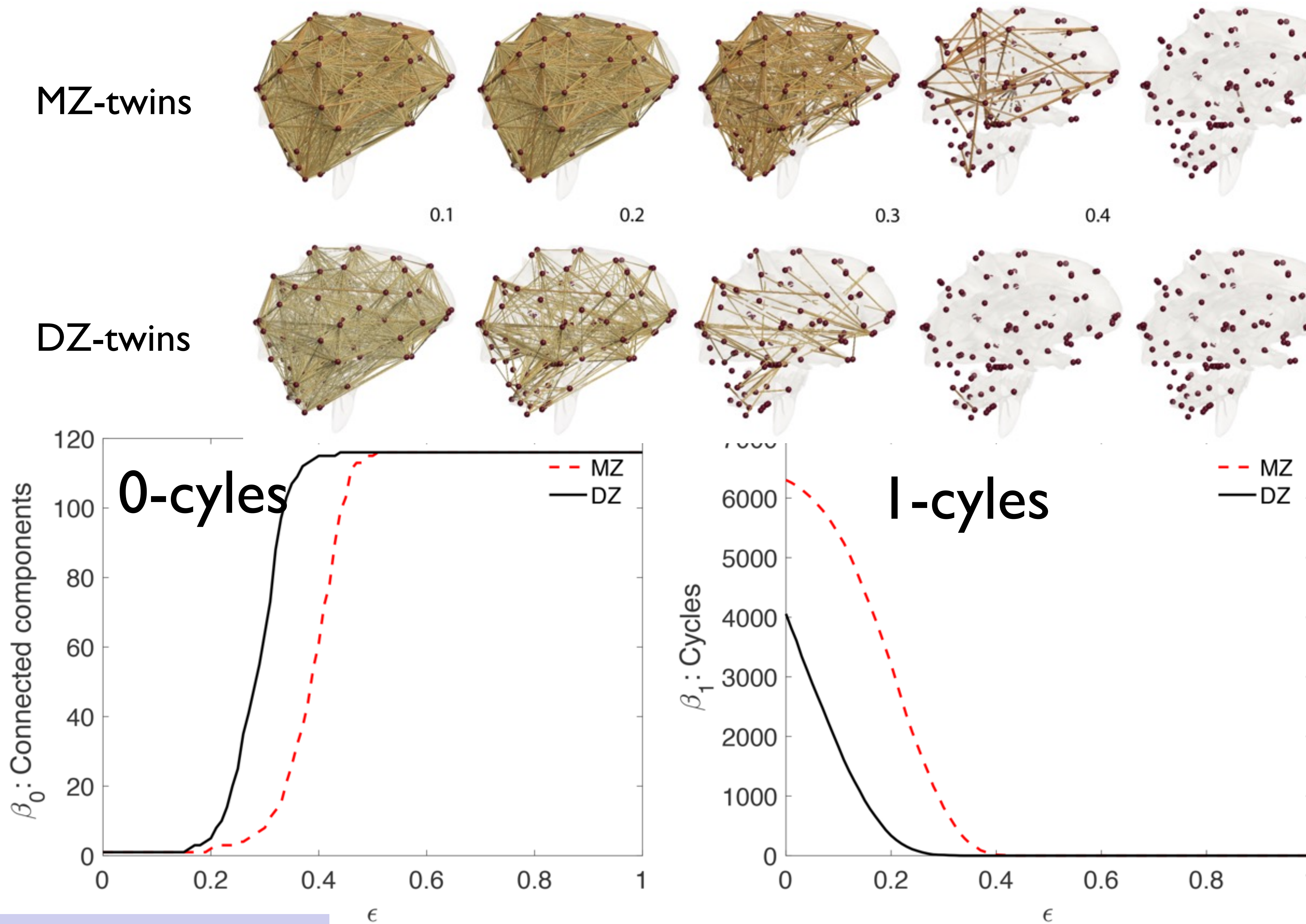
26 autism spectrum disorder (ASD) children

11 pediatric control subjects

PH_betti.m

Lee et al. (2011) ISBI

Genetic effect on Betti curves of rs-fMRI network



PH_betti.m

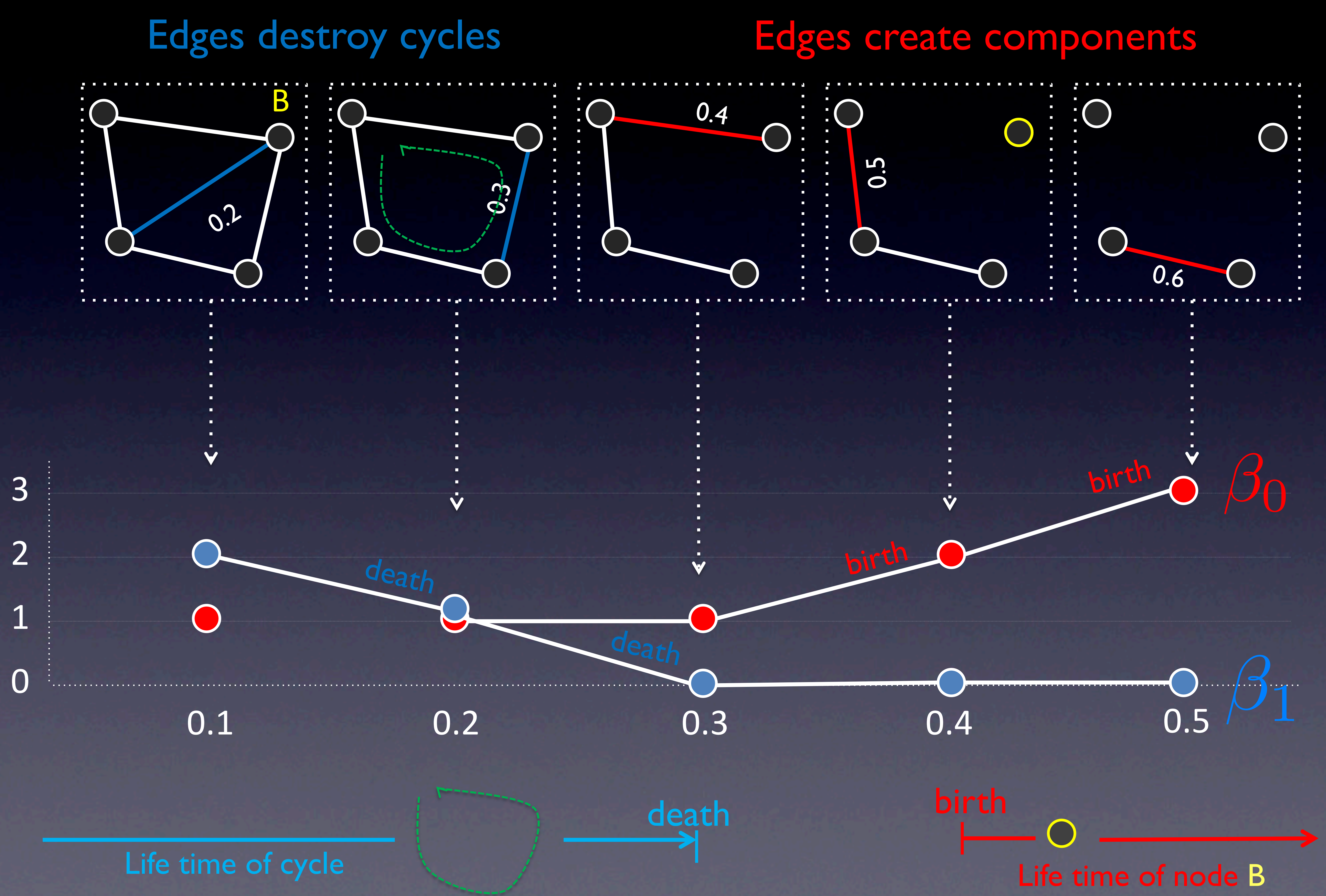
Chung et al. 2019 Network Neuroscience 3:674-

Birth and death decomposition

Songdechakraiwut et al. 2021 MICCAI 166-176

Songdechakraiwut and Chung. 2023, Annals of Appled Statistics

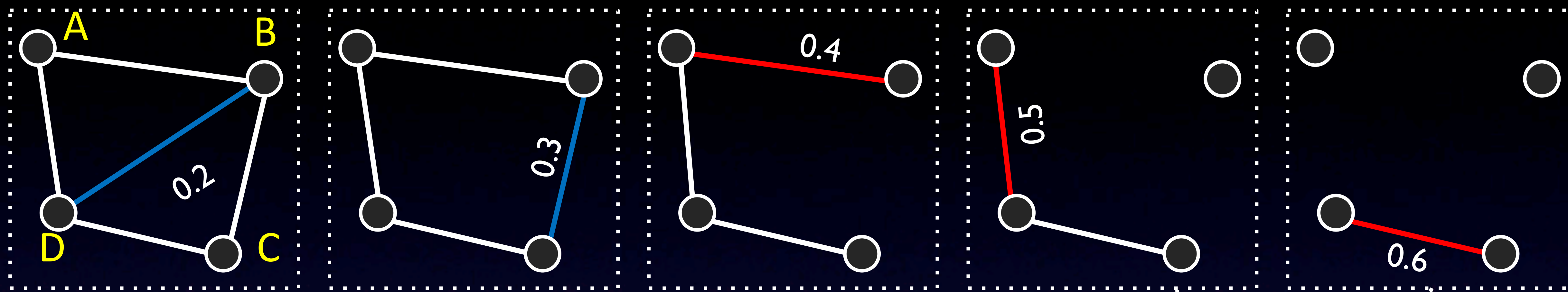
Persistence = Life time (death – birth) of a feature



Theorem *Birth & death sets partition* the edge set

E_1 Edges destroy cycles

E_0 Edges create components

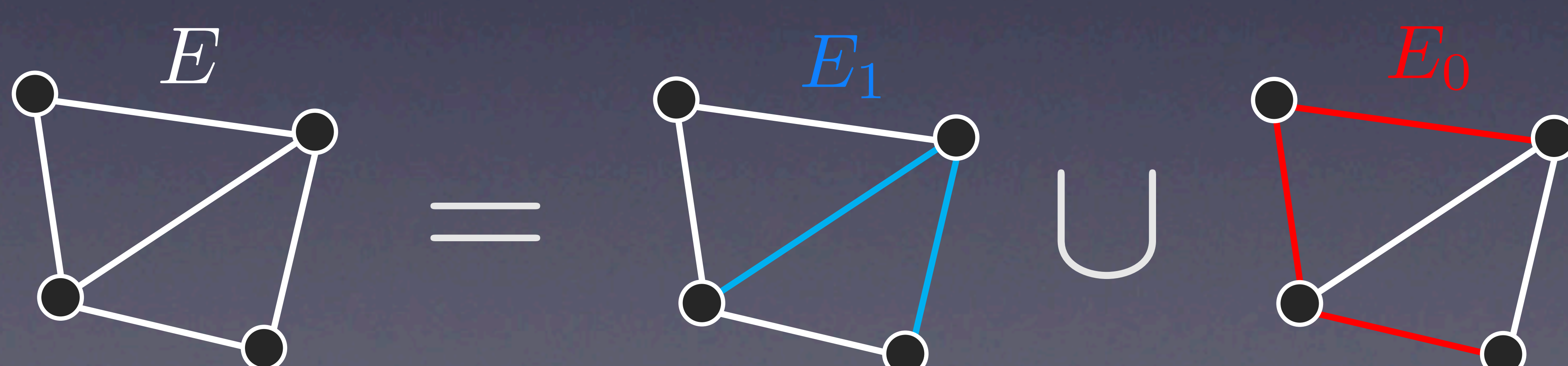


$$\#(E_1) = 1 + \frac{|V|(|V|-3)}{2}$$

$$\#(E_0) = |V| - 1$$

$$\#(E) = \frac{|V|(|V|-1)}{2}$$

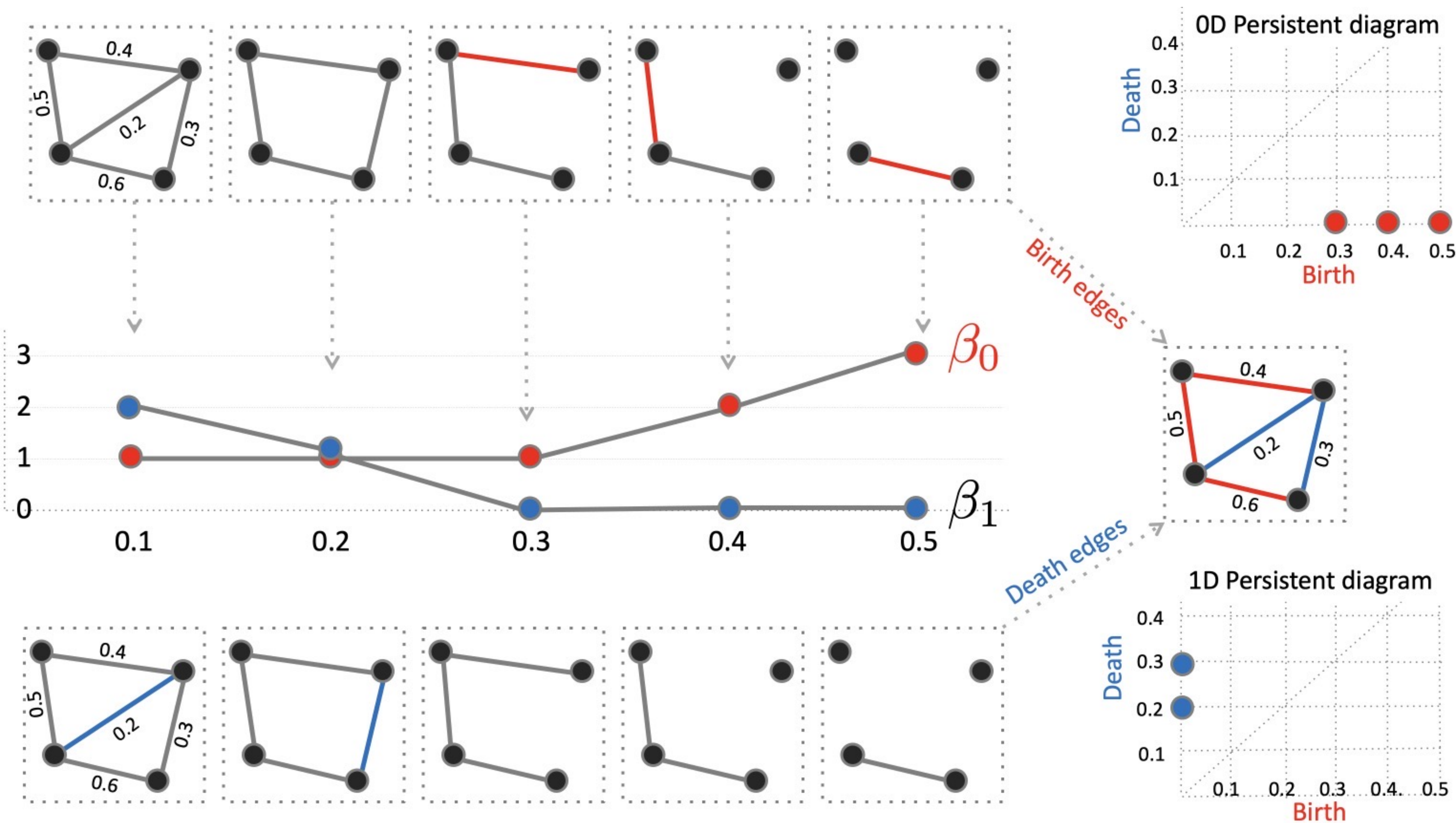
$$E = E_1 \cup E_0$$



Maximum spanning tree

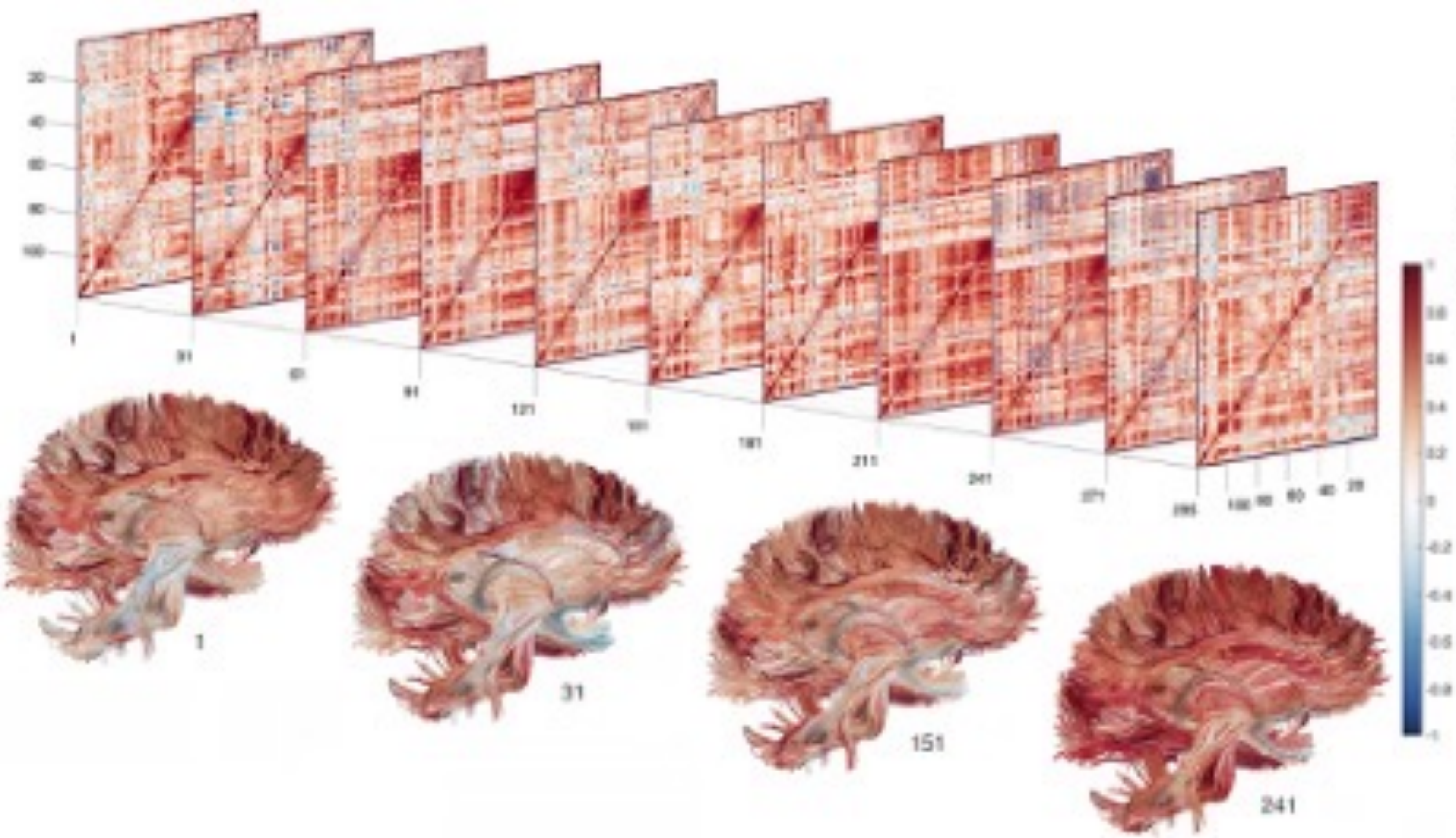
$$O(|E| \log |V|)$$

Songdechakraiwut & Chung 2020 arXiv: 2012.00675

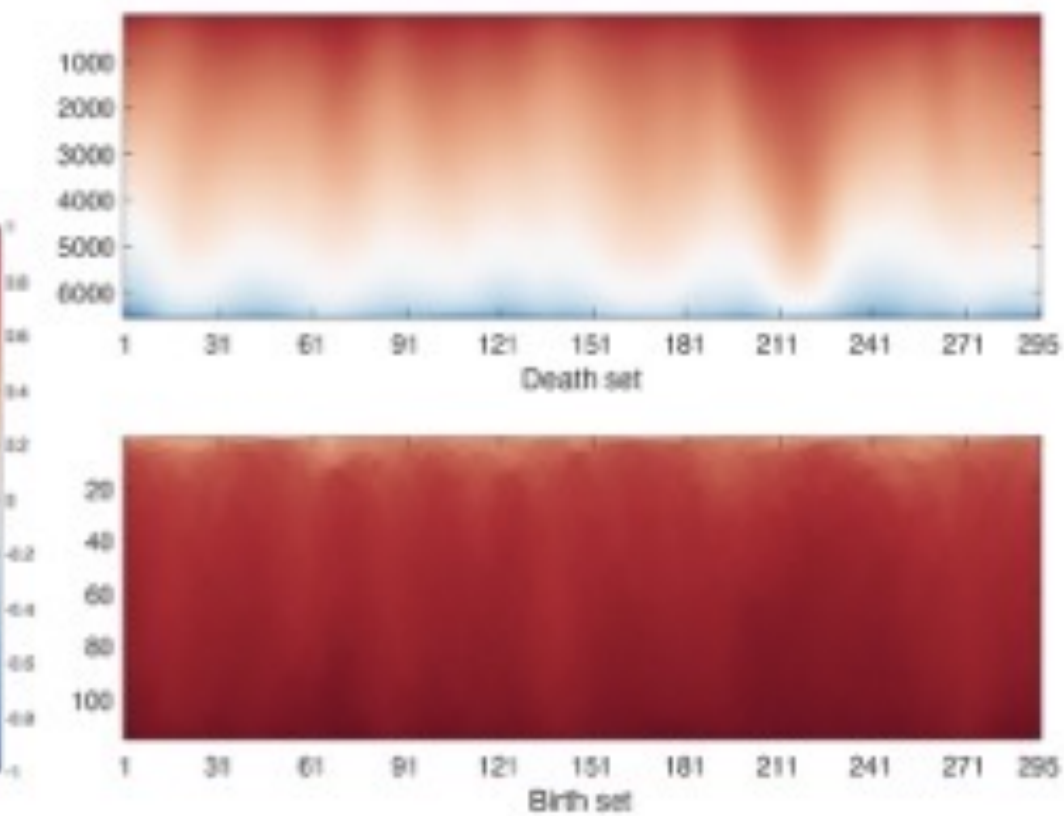


WS_decompose.m

Dynamically changing correlation network from rs-fMRI



Dynamically changing birth-death sets



WS_decompose.m

Topological inference

Songdechakraiwut and Chung. 2023, Annals of Appled Statistics

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

2-Wasserstein distance between persistent diagrams

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

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

Persistent diagrams

$$P_1 = \{x_1, \cdots, x_q\} \subset \mathbb{R}^2 \qquad P_2 = \{y_1, \cdots, y_q\} \in \mathbb{R}^2$$

Empirical distributions

$$f_1(x) = \frac{1}{q}\sum_{i=1}^{q} \delta(x - x_i) \qquad f_2(y) = \frac{1}{q}\sum_{i=1}^{q} \delta(y - y_i)$$

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

Assignment problem: Hungarian algorithm

$\mathcal{O}(q^3)$

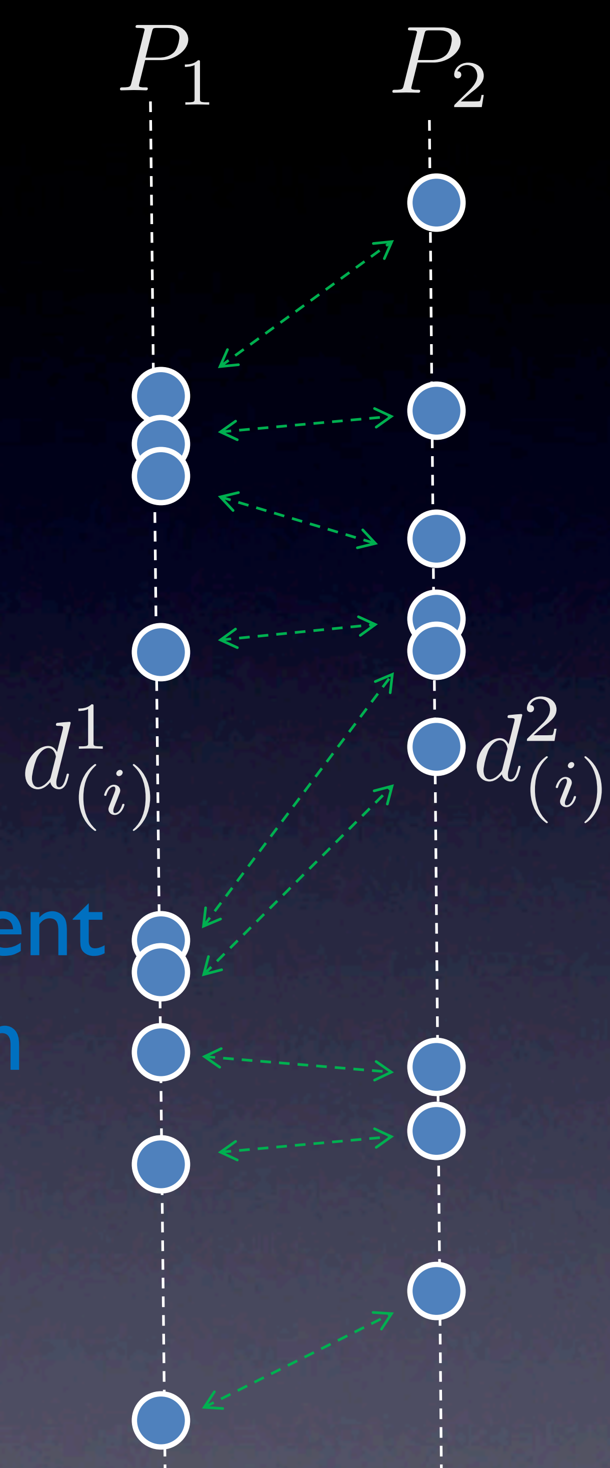
Graph filtration

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

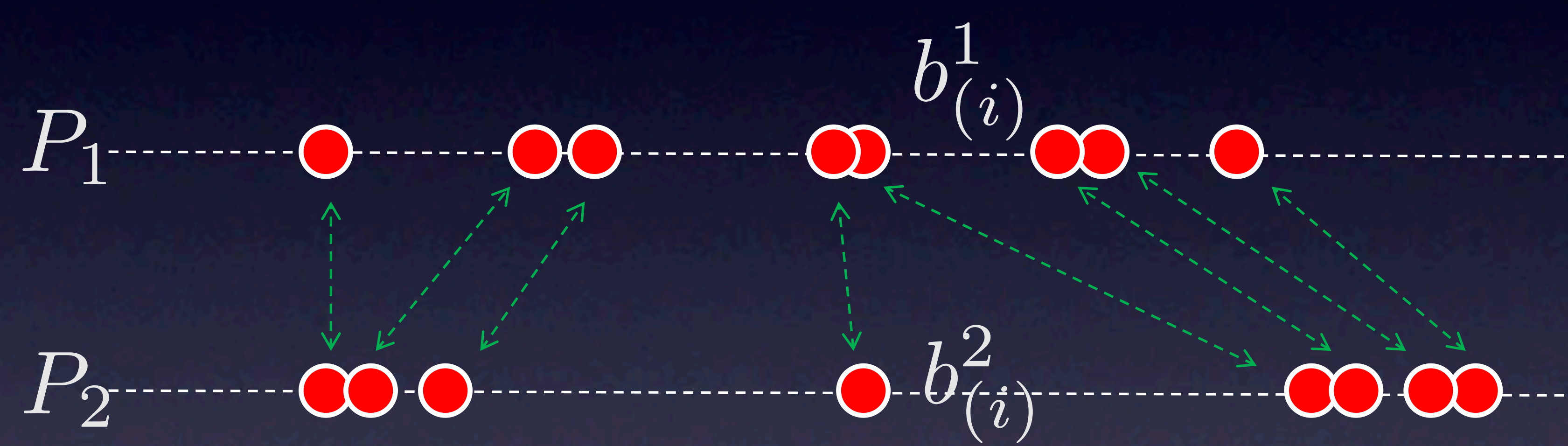
Wasserstein distance for graph filtrations

WS_pdist2.m

H_1 1D persistent diagram



H_0 0D persistent diagram



$$\mathcal{D}_0(P_1, P_2)^2 = \sum_i (b^1_{(i)} - b^2_{(i)})^2$$

$$\mathcal{D}_1(P_1, P_2)^2 = \sum_i (d^1_{(i)} - d^2_{(i)})^2$$

Songdechakraiwu & Chung 2023
Annals of Applied Statistics 17:403-433

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

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

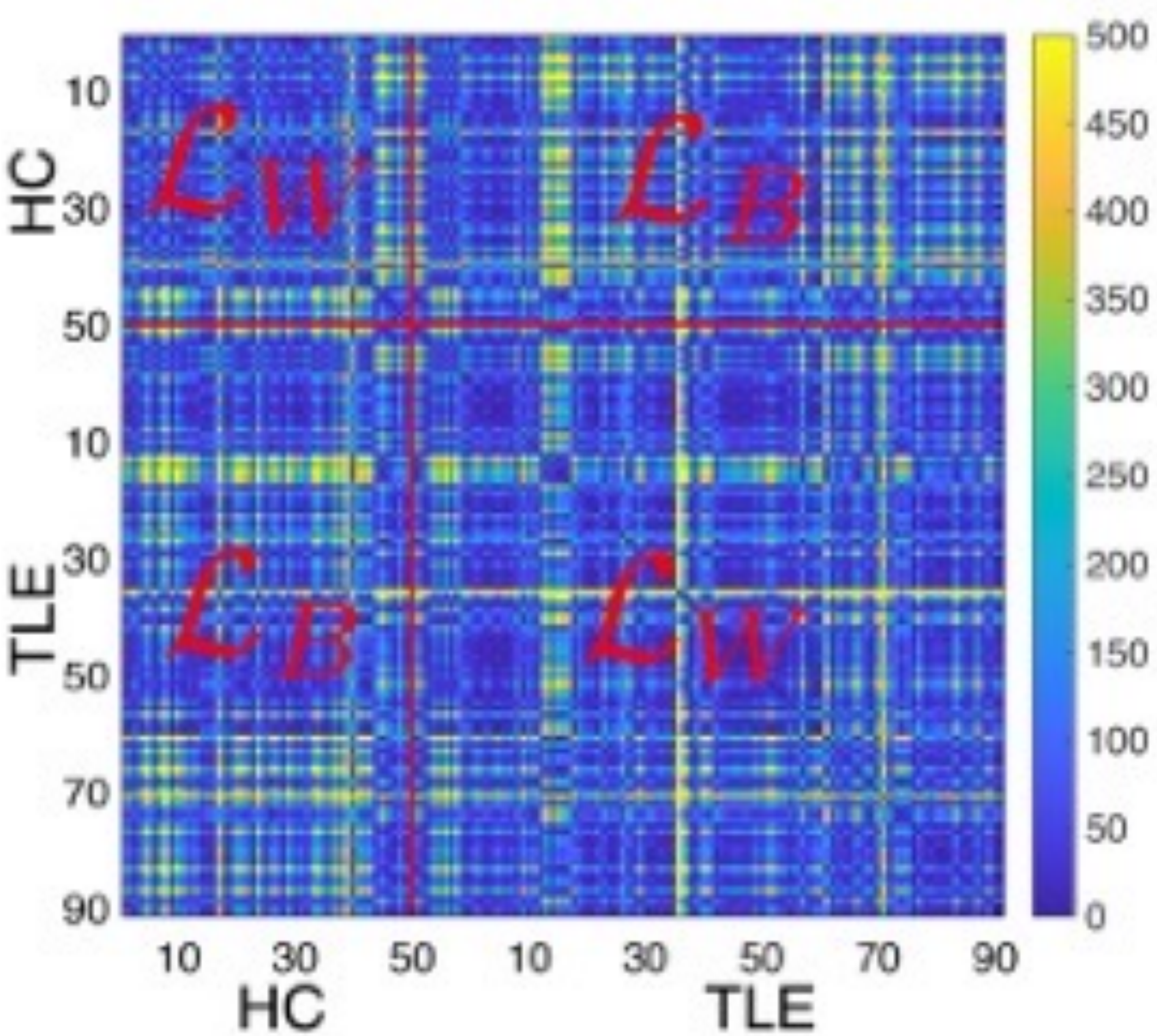
Statistic $\phi = \dfrac{l_B}{l_W}$

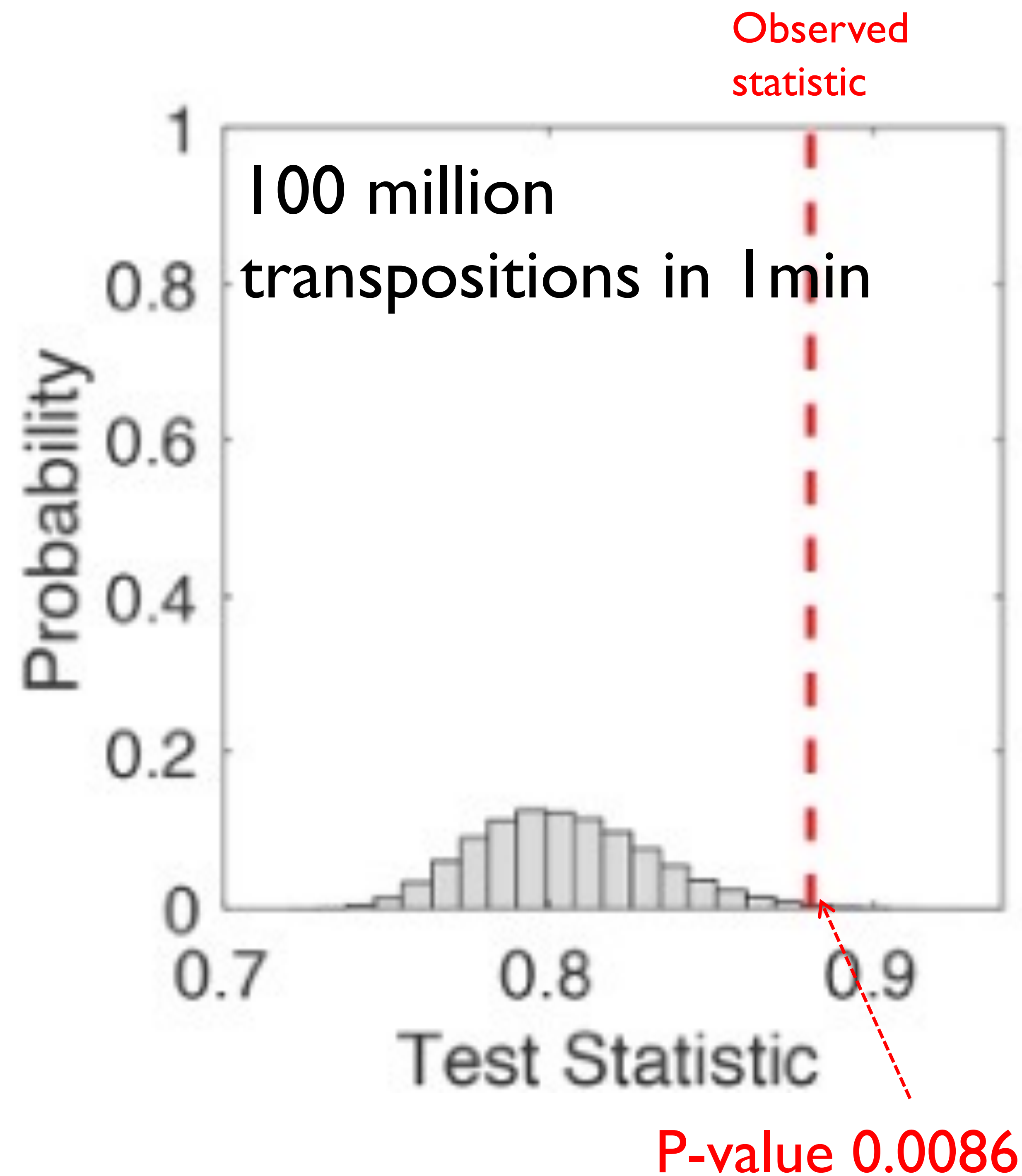
Small ϕ → small group separation

Large ϕ → large group separation

WS_ratio.m

Transposition test (online permutation test)



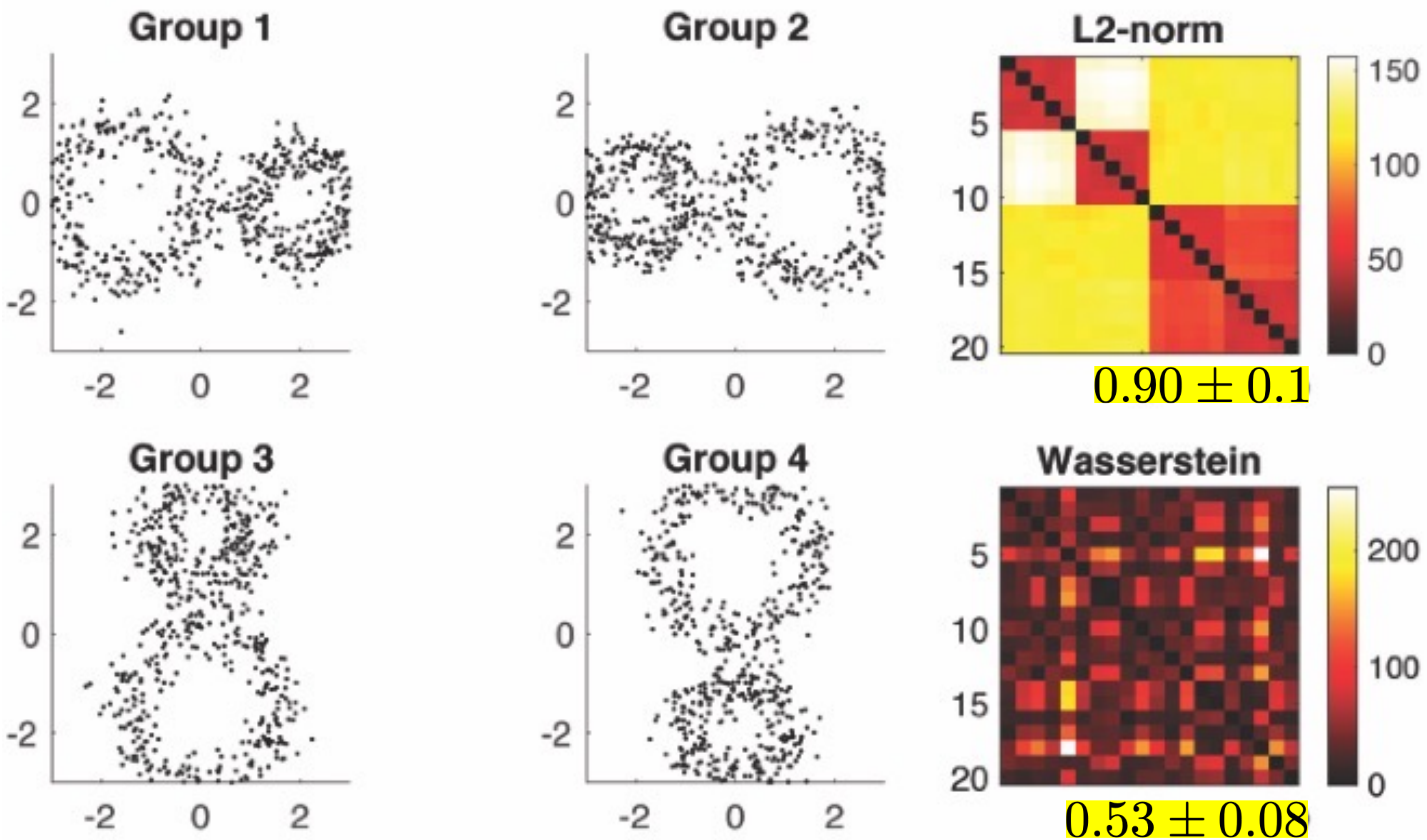


$$l_W \to l_W + \Delta(tranposition)$$

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

WS_transposition.m

Topologically invariant patterns



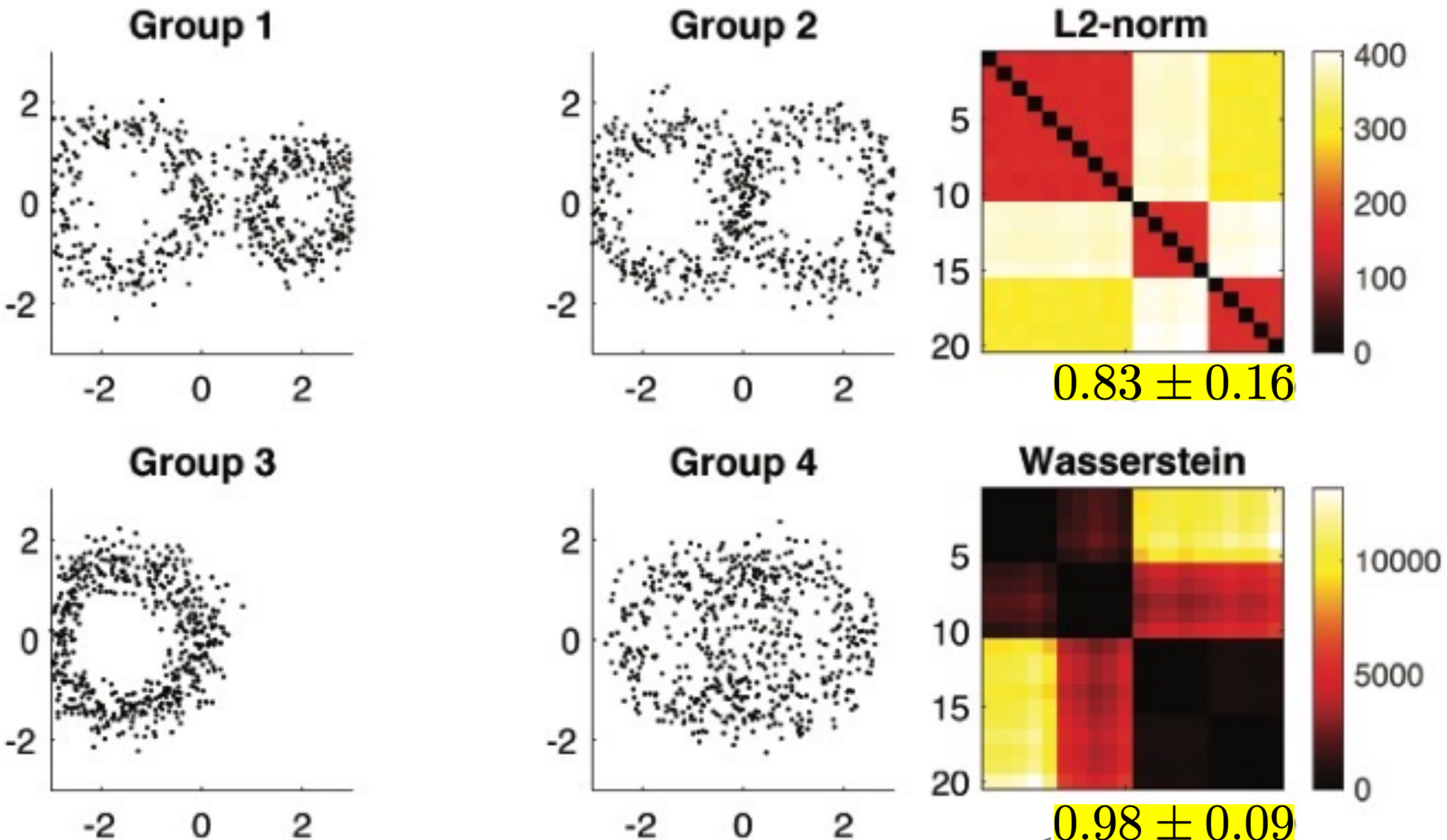
0.90 ± 0.1

0.53 ± 0.08

WS_cluster.m

Clustering accuracy

Topologically different patterns

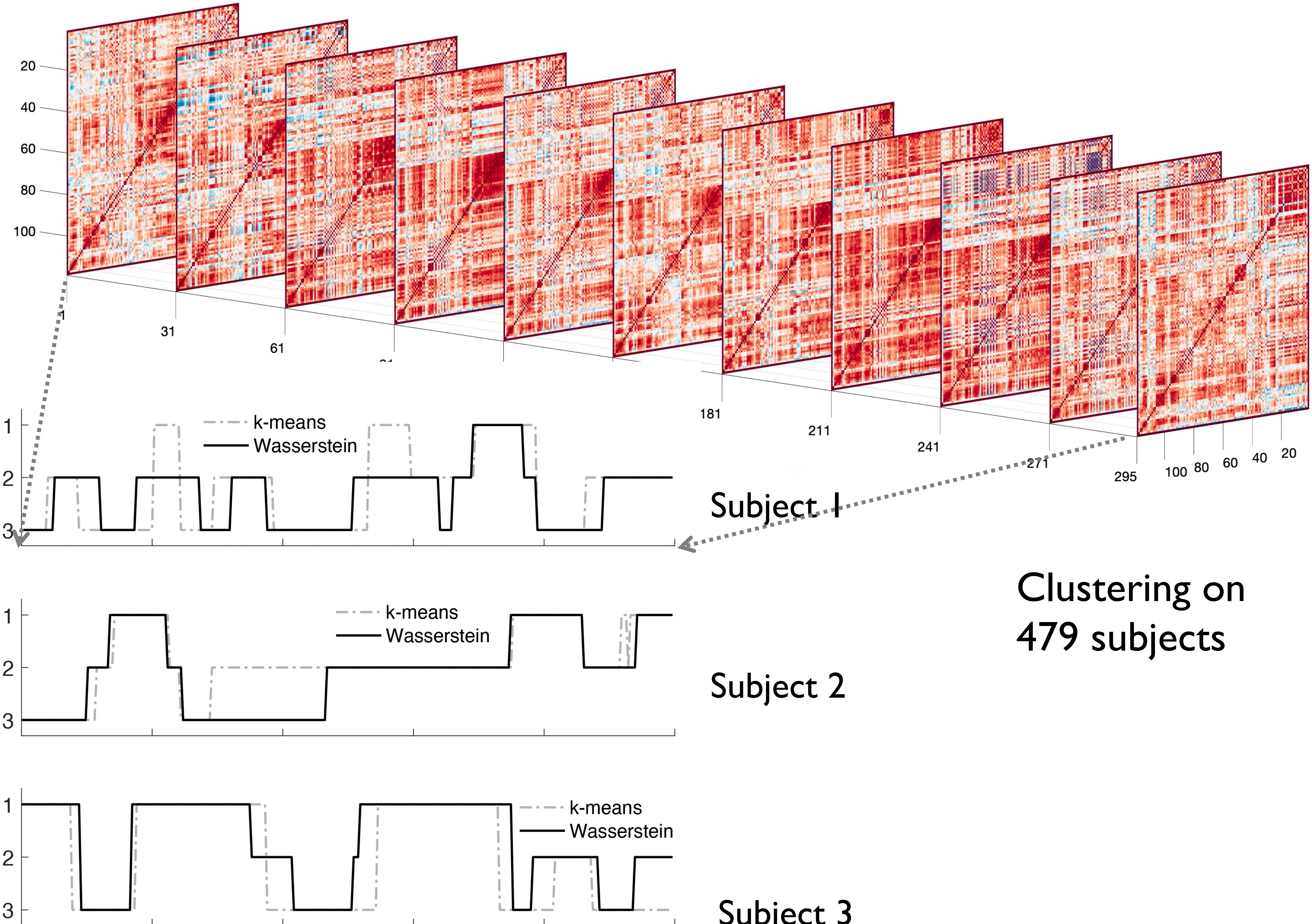


0.83 ± 0.16

0.98 ± 0.09

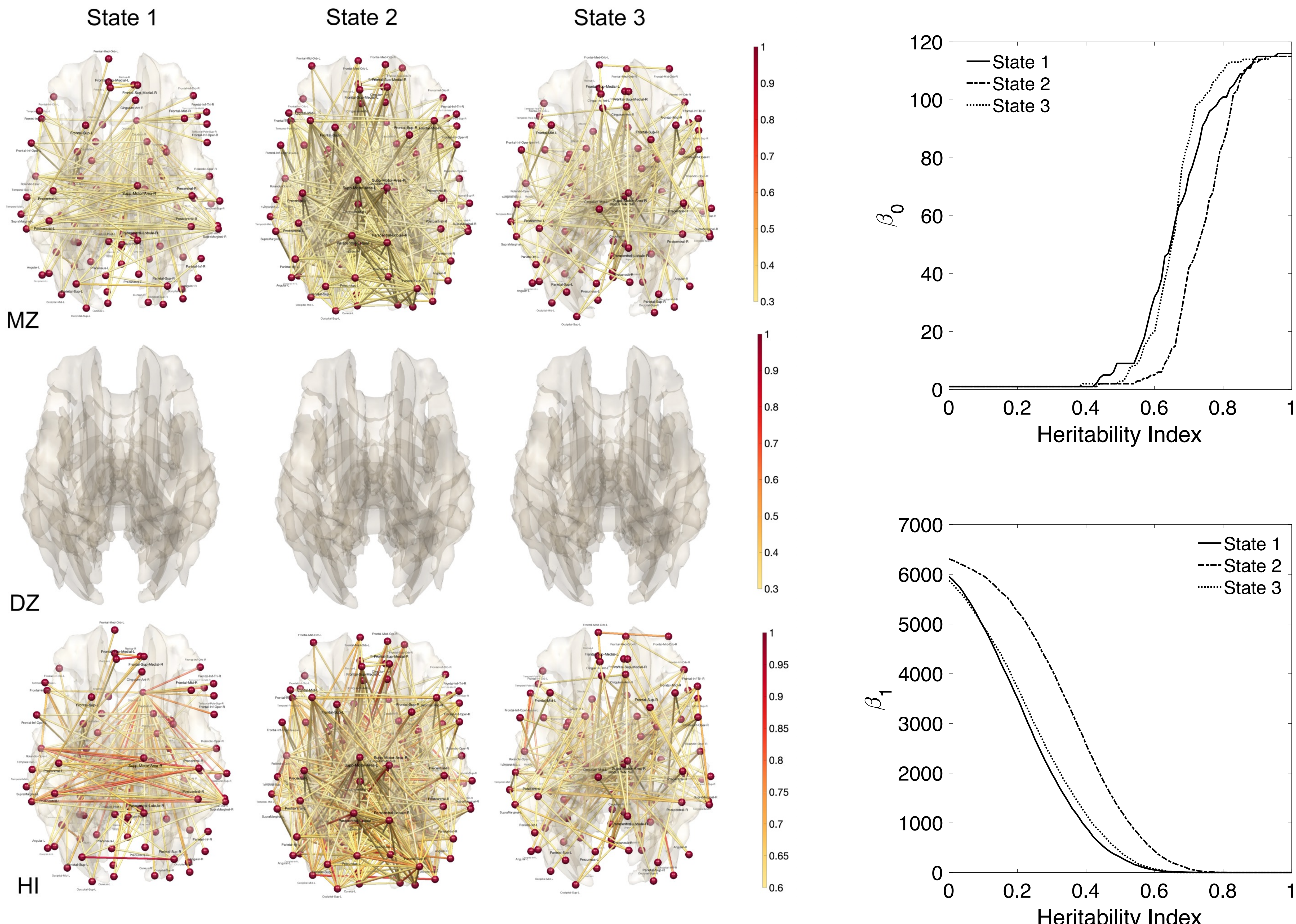
WS_cluster.m

Clustering accuracy



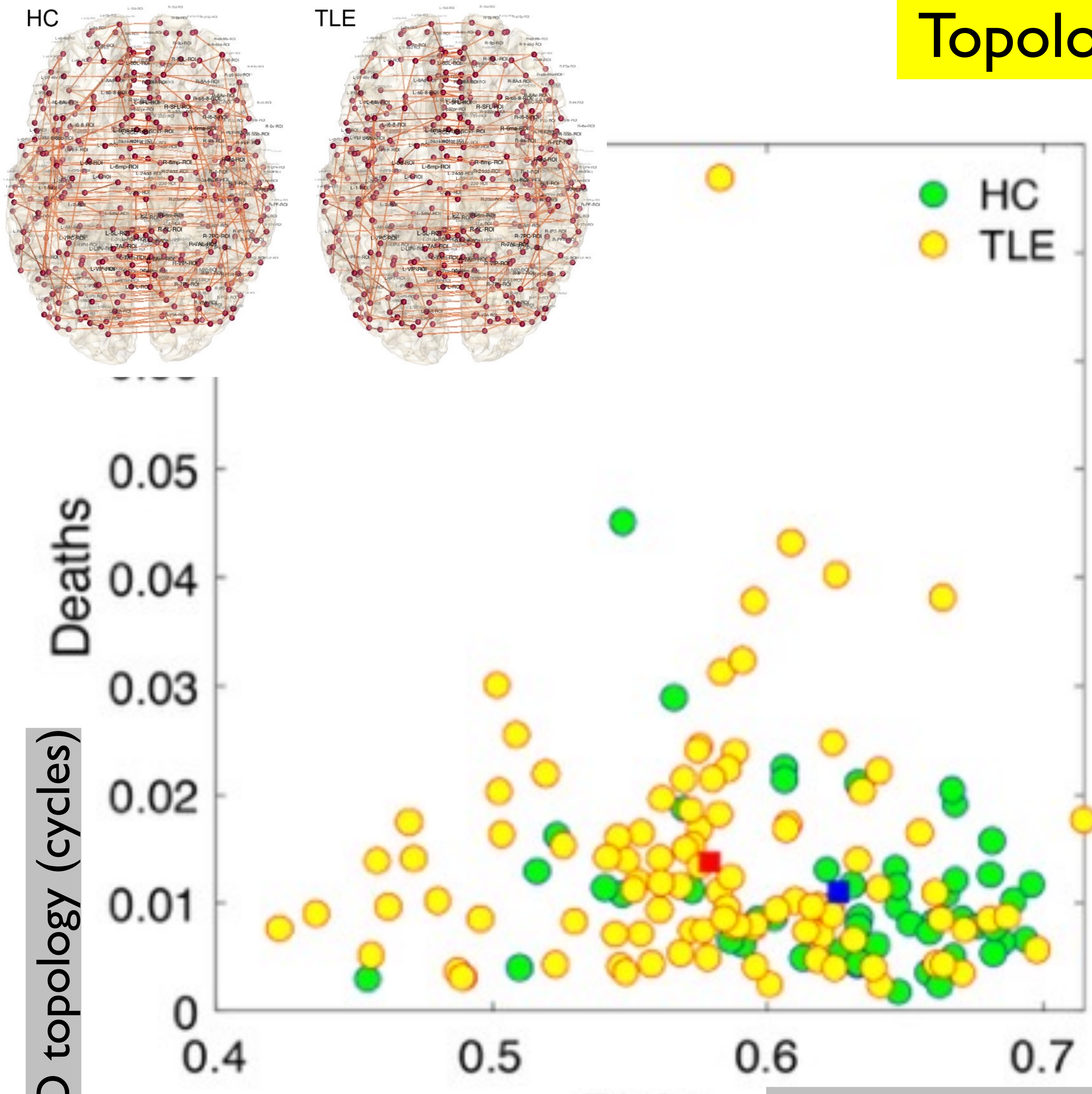
Clustering on 479 subjects

Heritability of state-space of rs-fMRI brain network



https://arxiv.org/pdf/2201.00087

Topological embedding



1D topology (cycles)

0D topology (connected components)

Healthy controls (HC)

Temporal lobe epilepsy (TLE)

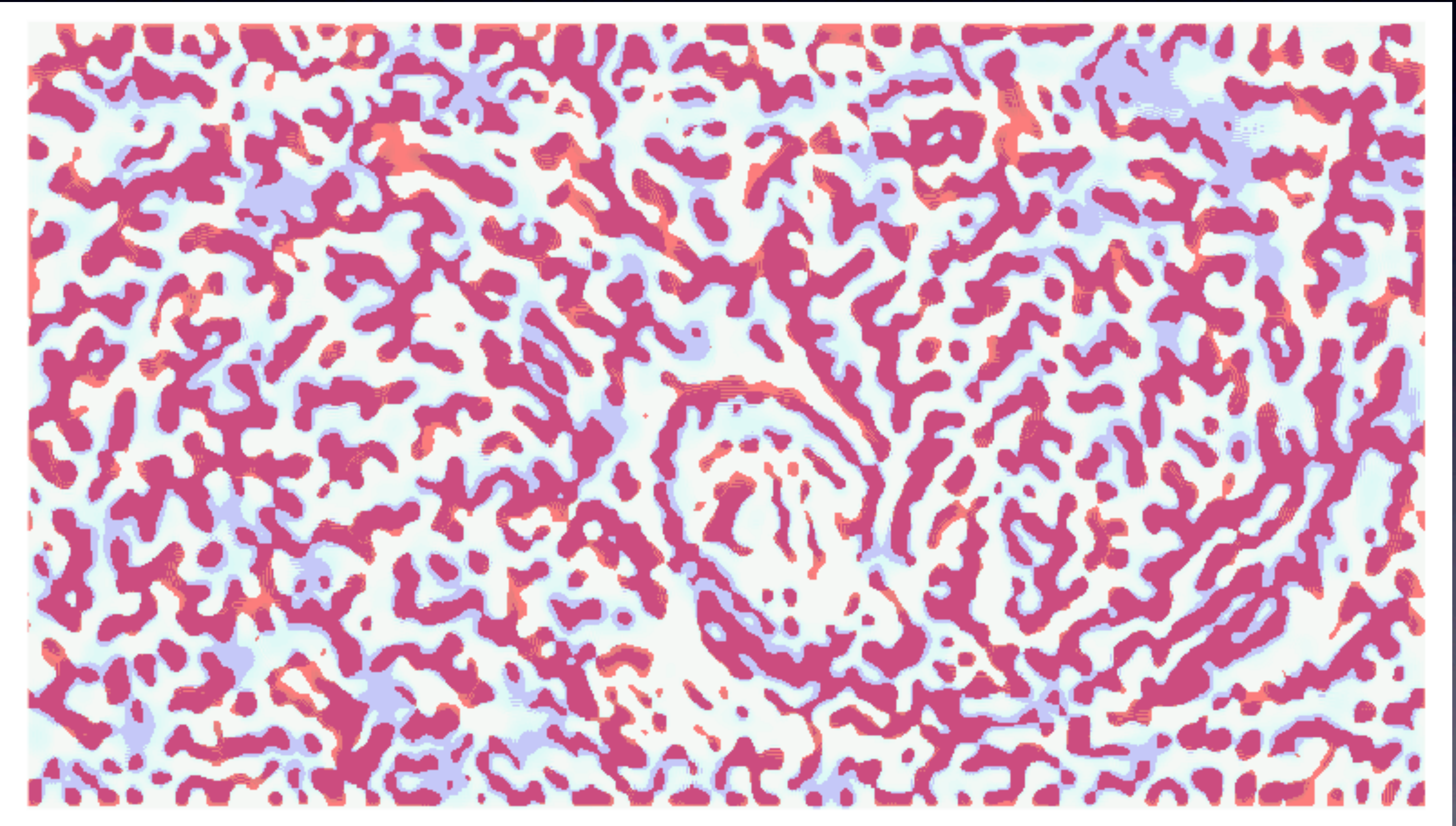
WS_embed.m

ISBI 2023 Friday 4:00-5:40pm

SALÓN BARAHONA 4

Special Session 6:

Wasserstein Distance in Biomedical Imaging



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 Info :

- Tomoo Yokoyama (Gifu University)
- Jongbaek Song (KIAS)
- Mason Poter (UCLA)
- Keunsu Kim (POSTECH)
- Peter Bubenik (University of Florida)
- Tamal K. Dey (Purdue University)
- Yuan Wang (University of South Carolina)
- Guowei Wei (Michigan State University)
- Alexander Strang (Chicago University)
- Mathieu Carriere (INRIA)
- Heather Harrington (Oxford University)

Thank you.

Inquiry, suggestion for PH-STAT, suggestions → mkchung@wisc.edu

We are located here. Join us for *postdoc* and *graduate research*