

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>

Acknowledgement

Zijian Chen, Tahmineh Azizi, Vijay Anand D, Sixtus Dakurah, Soumya Das, Tananun Songdechakriwut,
Univ. of Wisconsin-Madison, US

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

Anass El Yaagoubi Bourakna, Hernando Ombao KAUST,
Saudi Arabia

Hyekyung Lee, Dong Soo Lee Seoul National University,
Korea

Grants: NIH R01 EB022856, R01 EB028753, NSF DMS-2010778

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

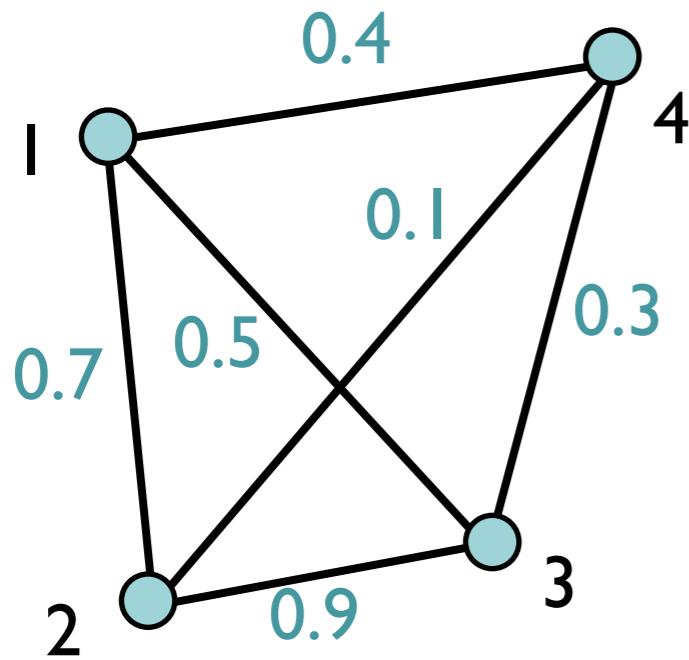
Persistent Homology

- 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

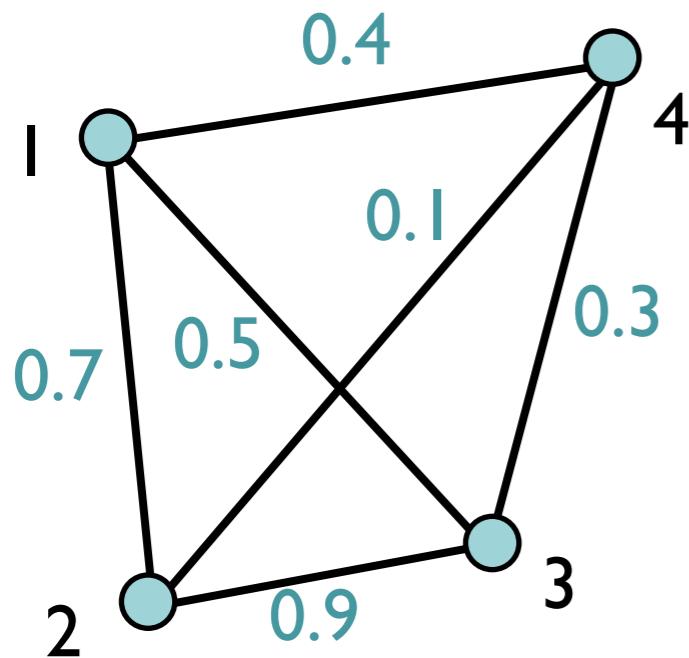
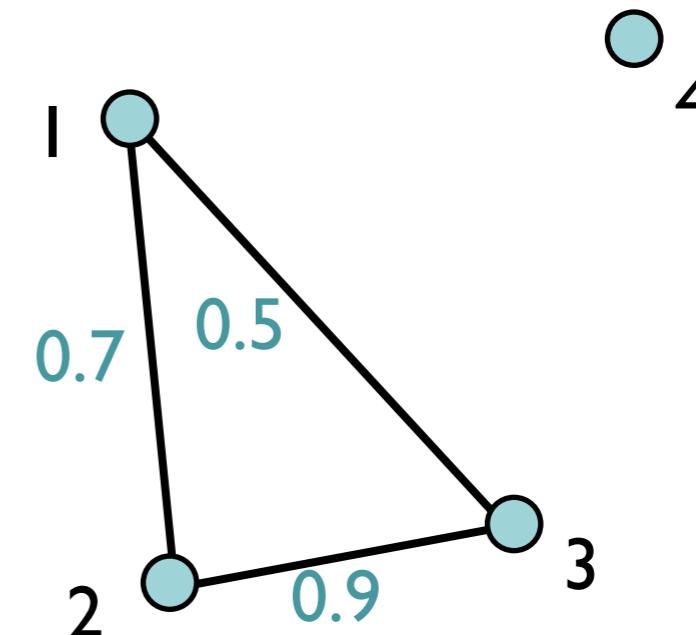
What is wrong with standard brain network analysis?

Edge weight ρ_{ij} between node i and j

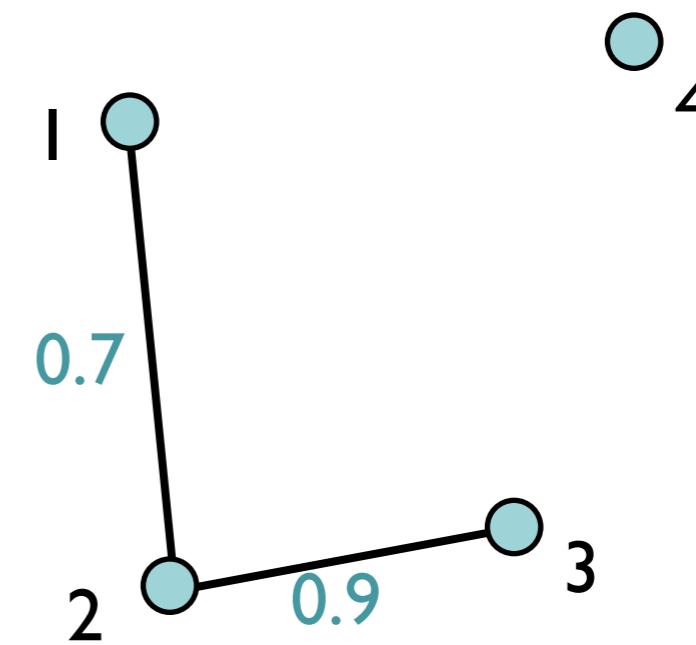
→ Connectivity matrix $\rho = (\rho_{ij})$



Threshold at 0.5

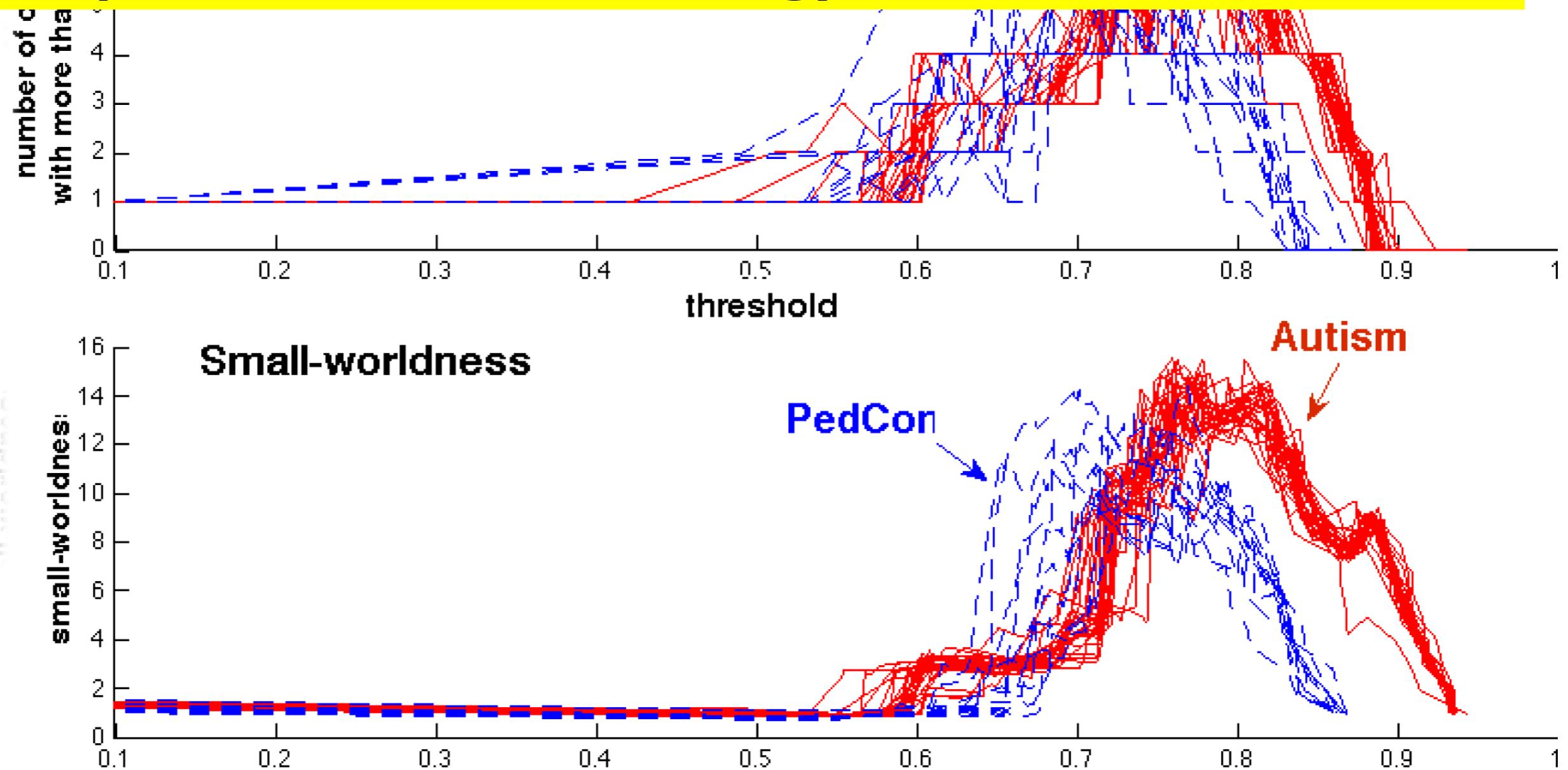


Threshold at 0.7

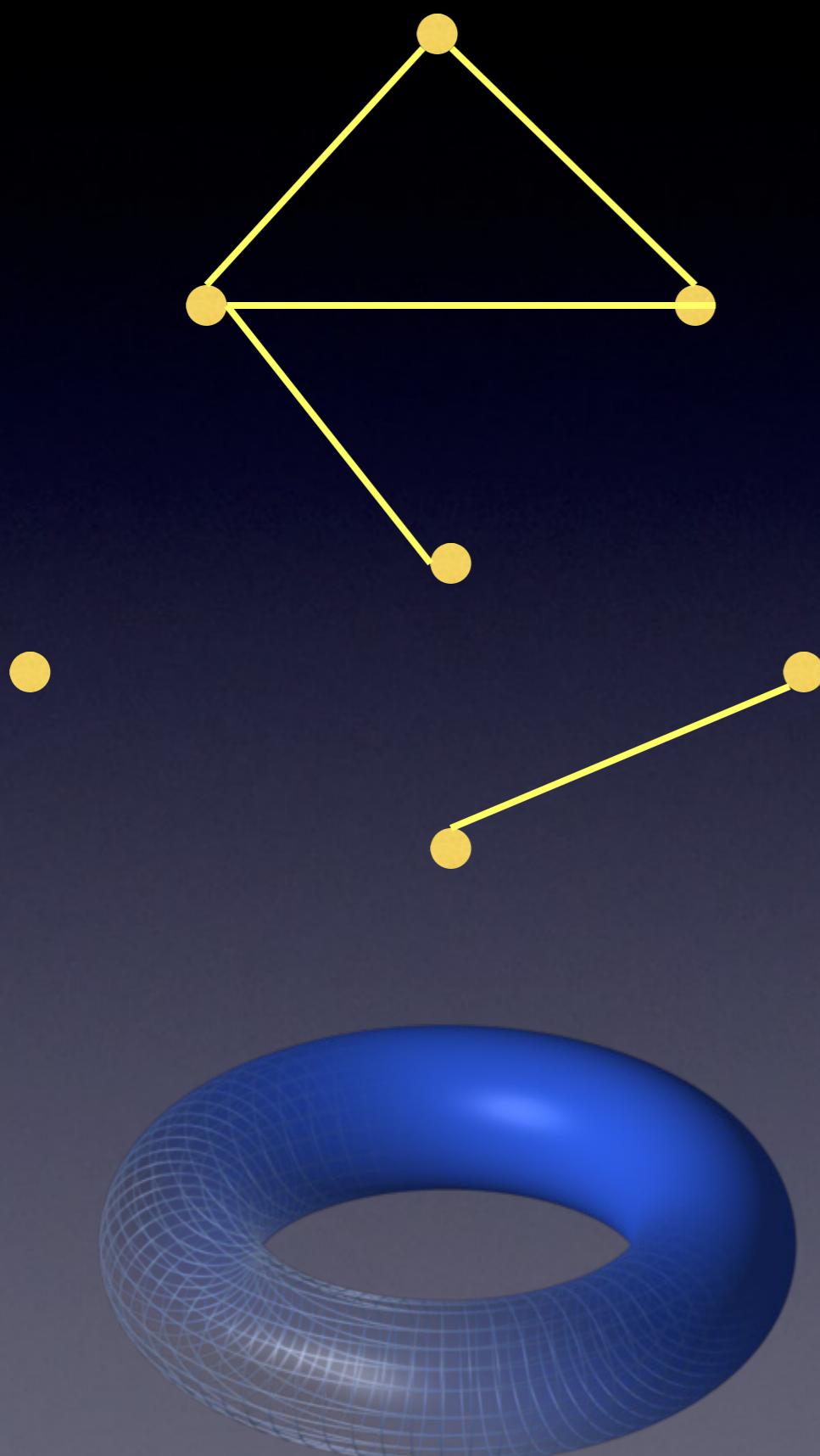


Single threshold often suboptimal → multiple thresholds

**What if we use every possible threshold
→ persistent homology**



Betti numbers β_i # of i-dimensional holes/loops

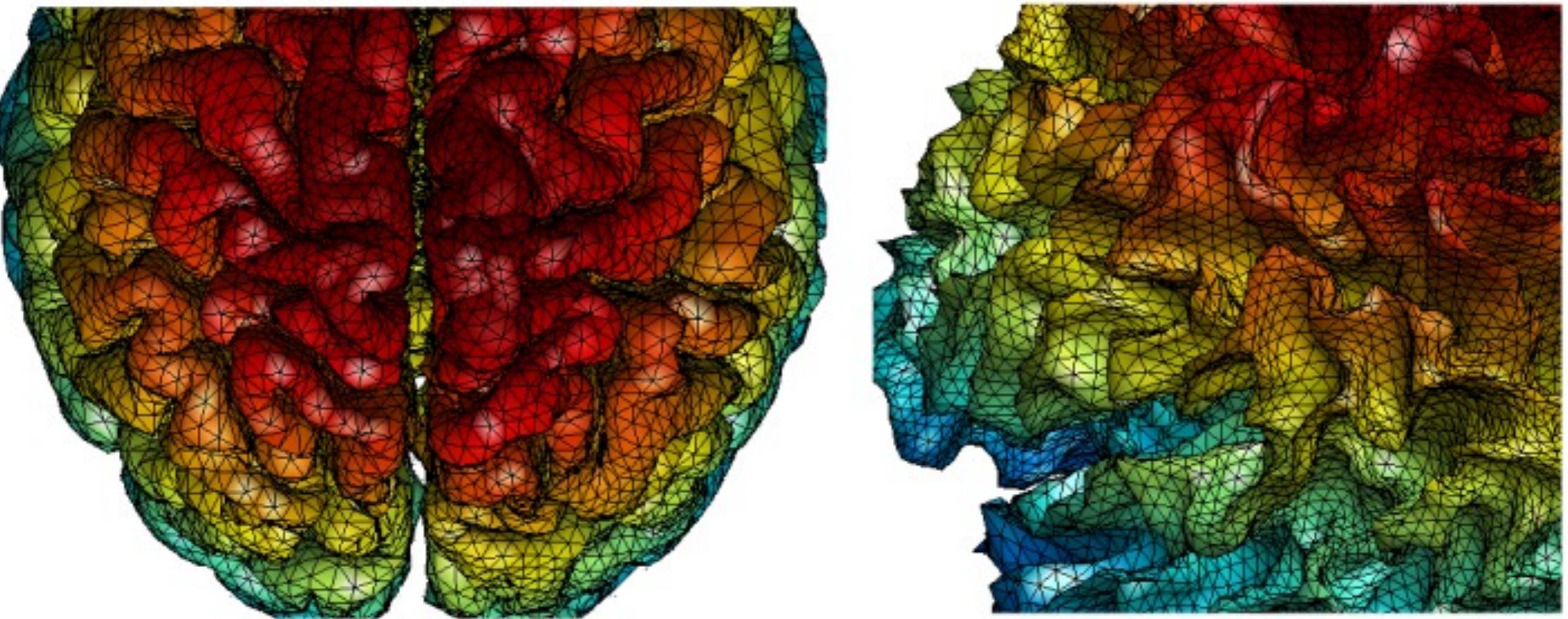


$\beta_0 = \# \text{ of connected components} = 3$
 $\beta_1 = \# \text{ of 1D holes} = 1$
 $\beta_2 = \# \text{ of 2D cavities} = 0$

Betti-number representation:
 $(3, 1, 0, 0, \dots)$

Euler characteristic:
 $\chi = \beta_0 - \beta_1 = 2$

$\beta_0 = 1, \beta_1 = 2, \beta_2 = 1$
 $(1, 2, 1, 0, 0, \dots)$



Euler characteristic of a surface mesh from SurfStat

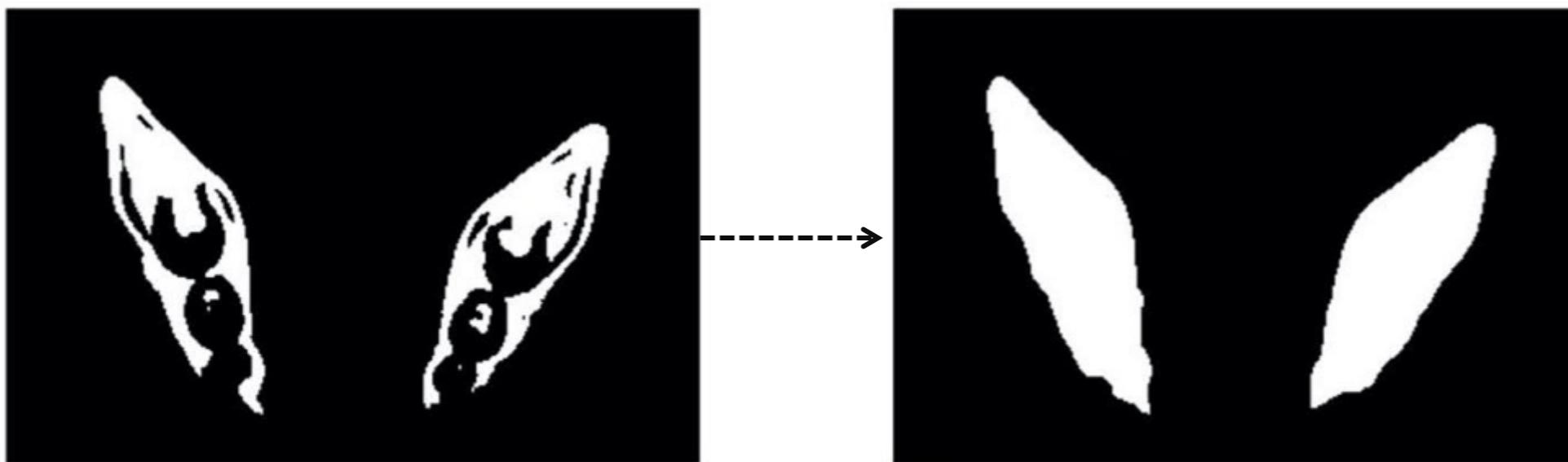
$N - E + F = 2$ for a surface topologically equivalent to a sphere.

For each triangle, there are three edges. Since two adjacent triangles share the same edge, the total number of edges is

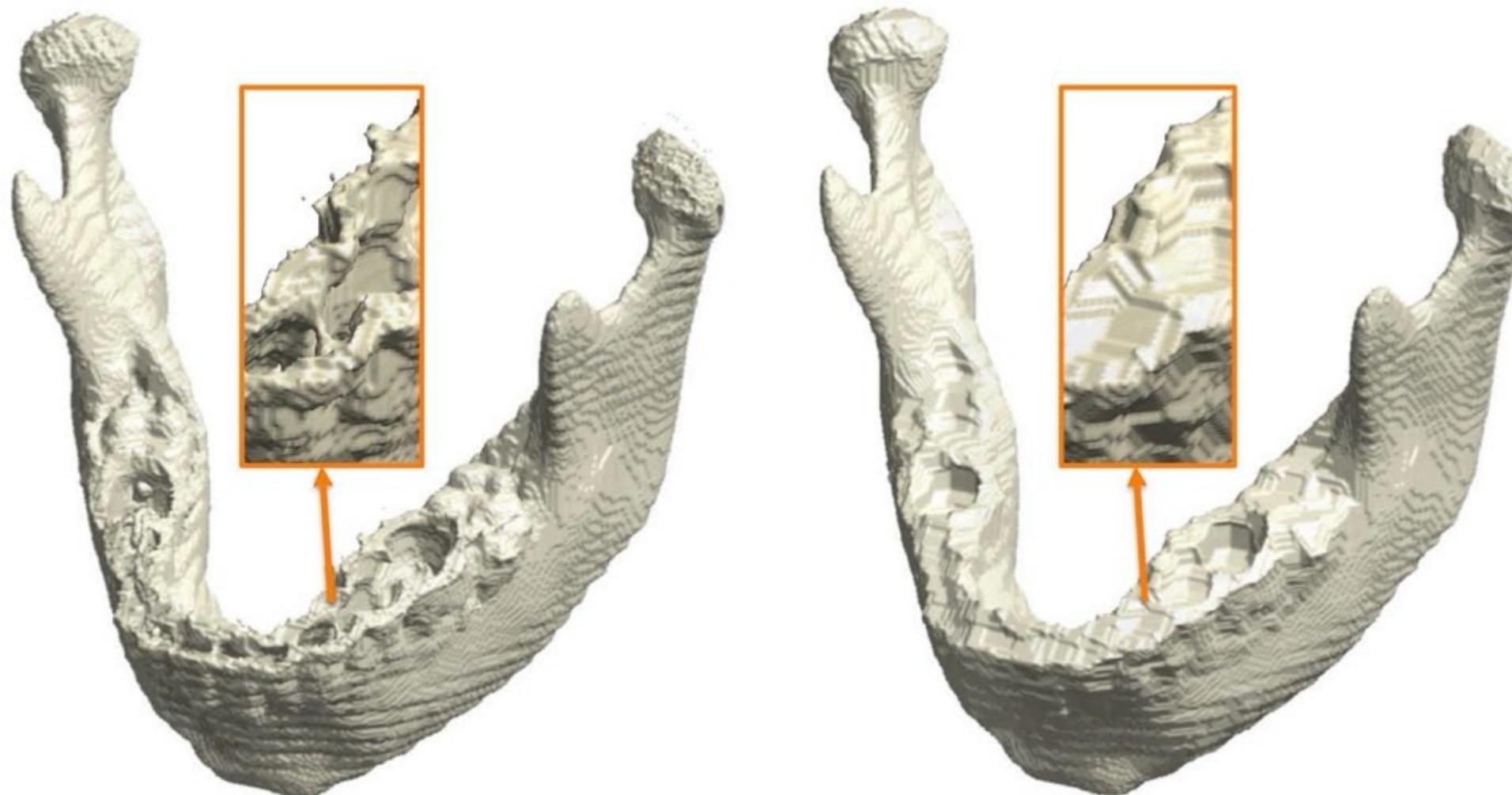
$$E = 3F/2 \rightarrow F=2N - 4 \text{ for a closed surface.}$$

Can be used to correct topological artifacts in FreeSurfer

Topology correction in CT segmentation



Hole & handles corrected using Euler characteristic



Keith Worsley's random field theory

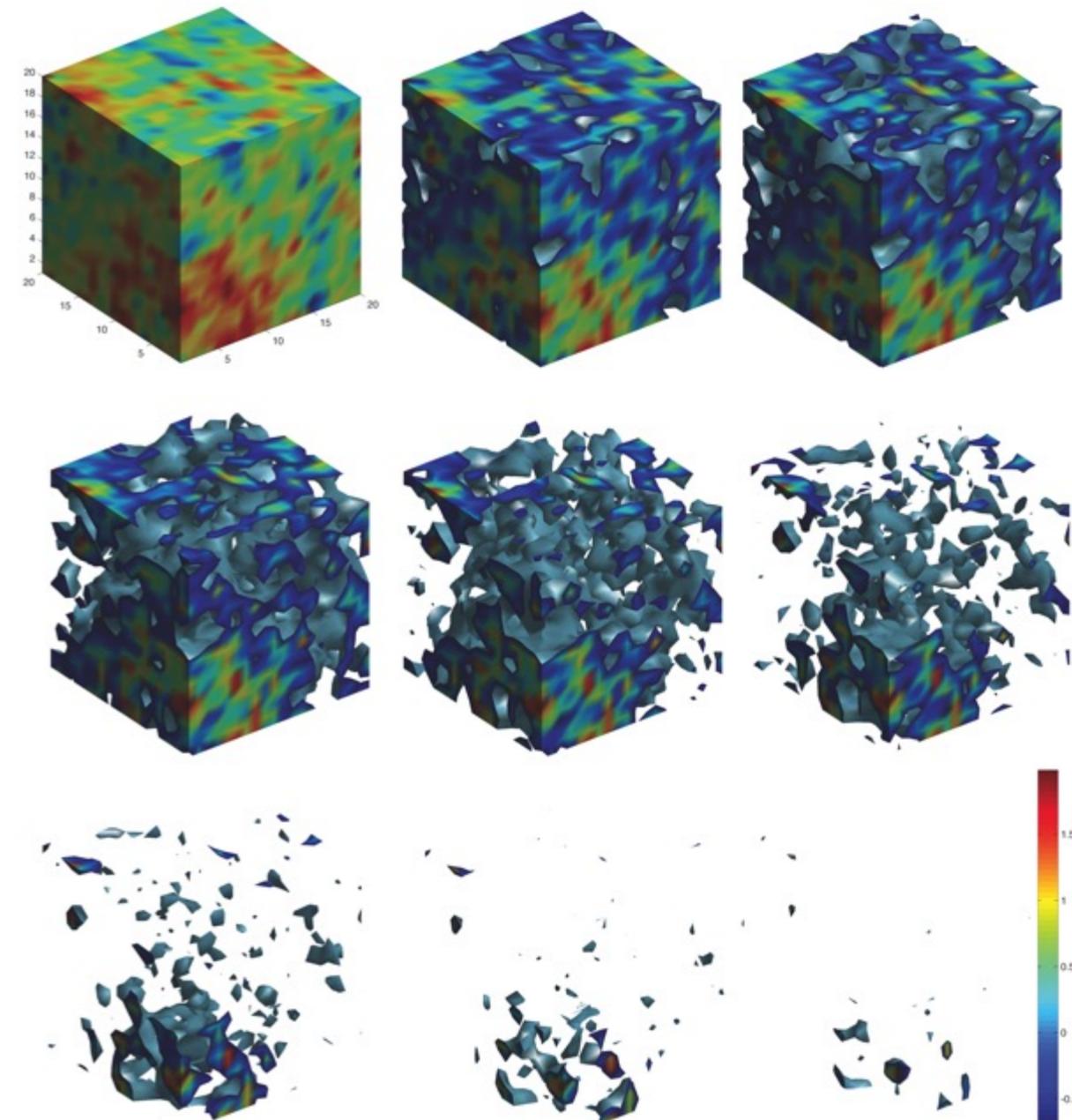
Random field

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

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

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

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



Milnor 1963 Morse theory

Adler, 1994 The geometry of random fields

Worsley et al., 1996 Human Brain Mapping

Morse Filtration

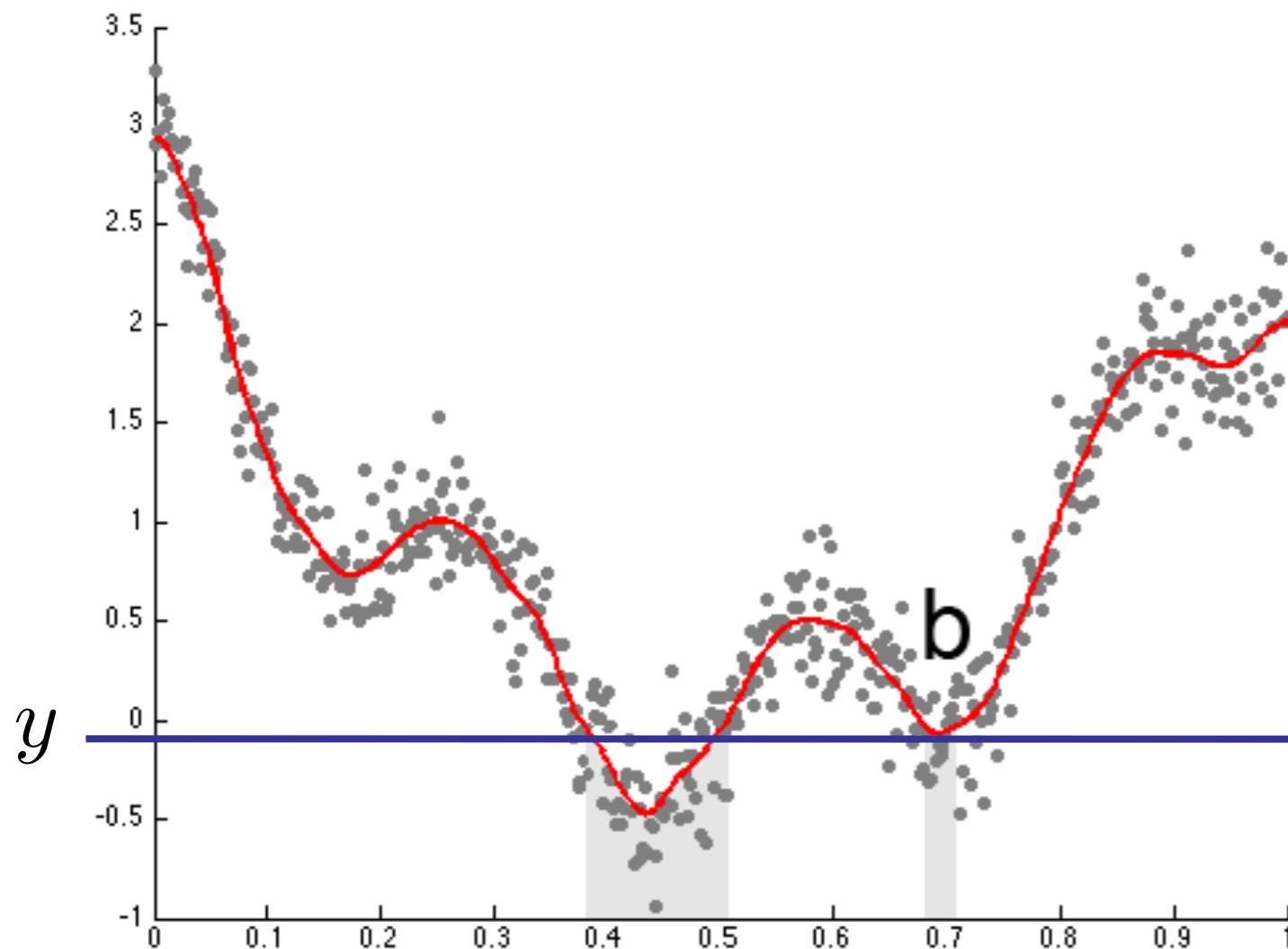
Chung et al., 2009 *Information Processing
in Medical Imaging (IPMI)* 5636:386-397.

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

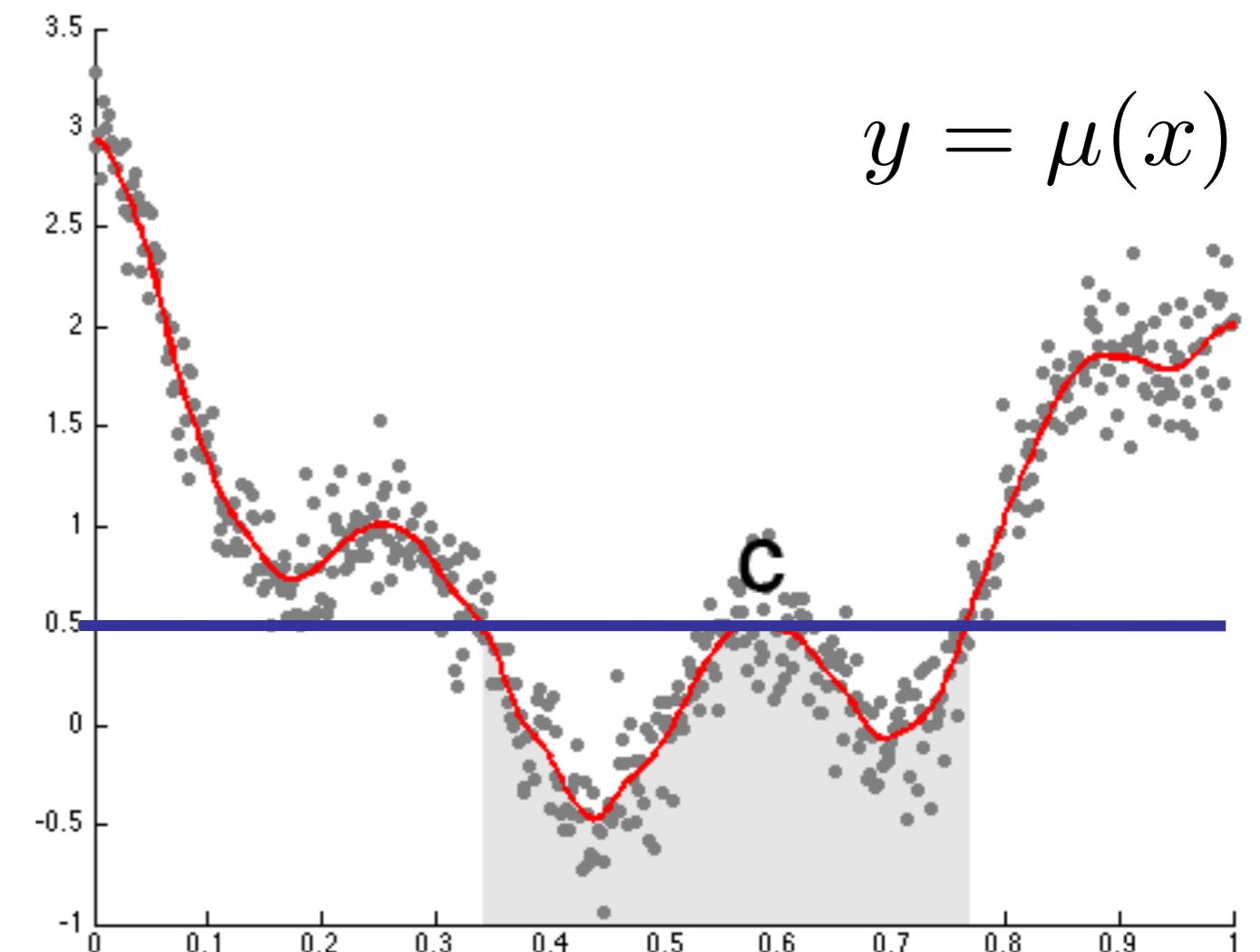
Morse filtration

Sublevel set

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

Morse filtration

$$R_b \subset R_c$$



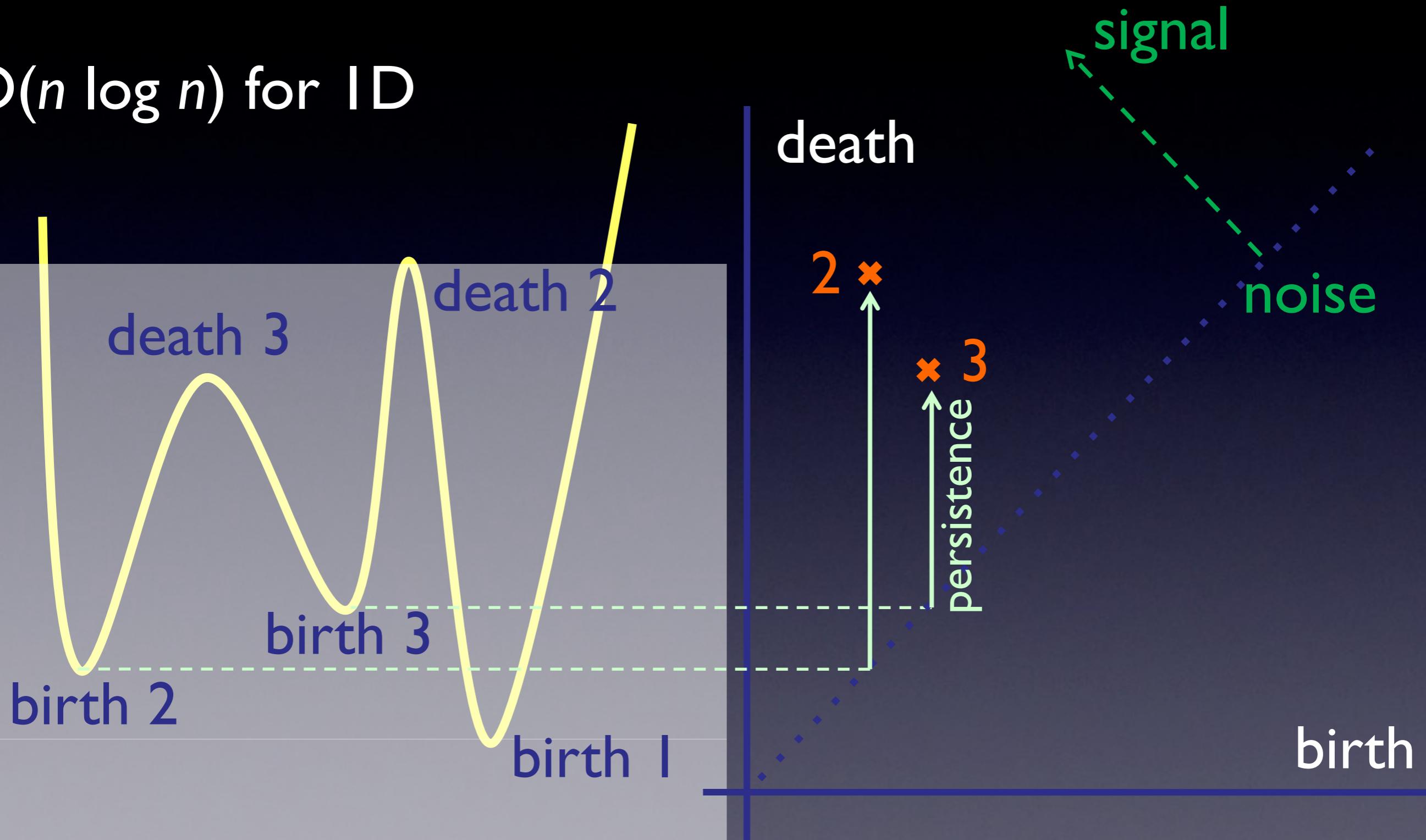
Component dies at c

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

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Persistence Diagram (PD)

$O(n \log n)$ for ID



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.

Surface Data

L. Kim⁴

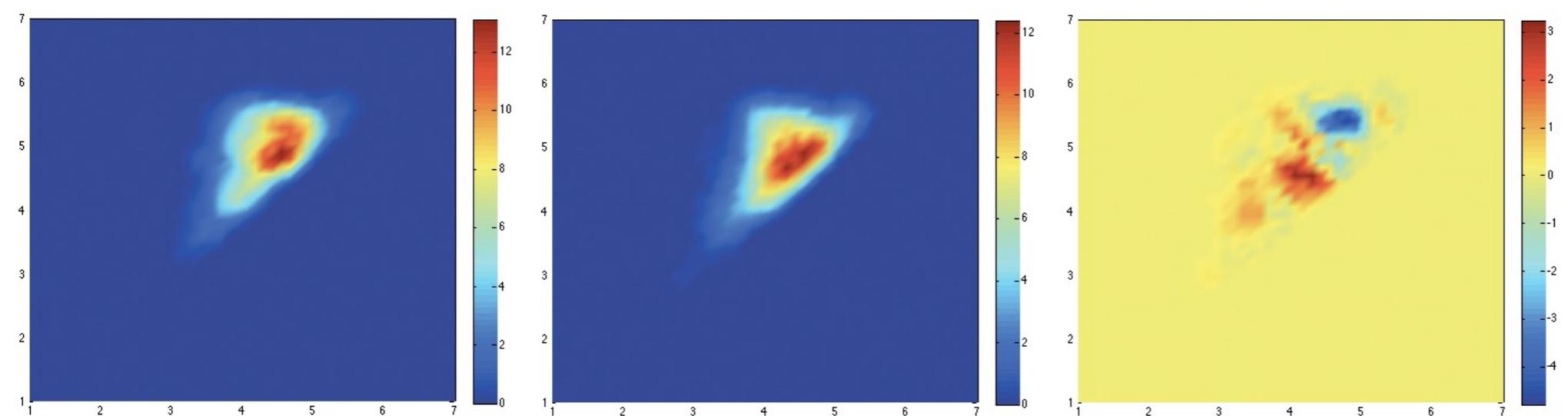
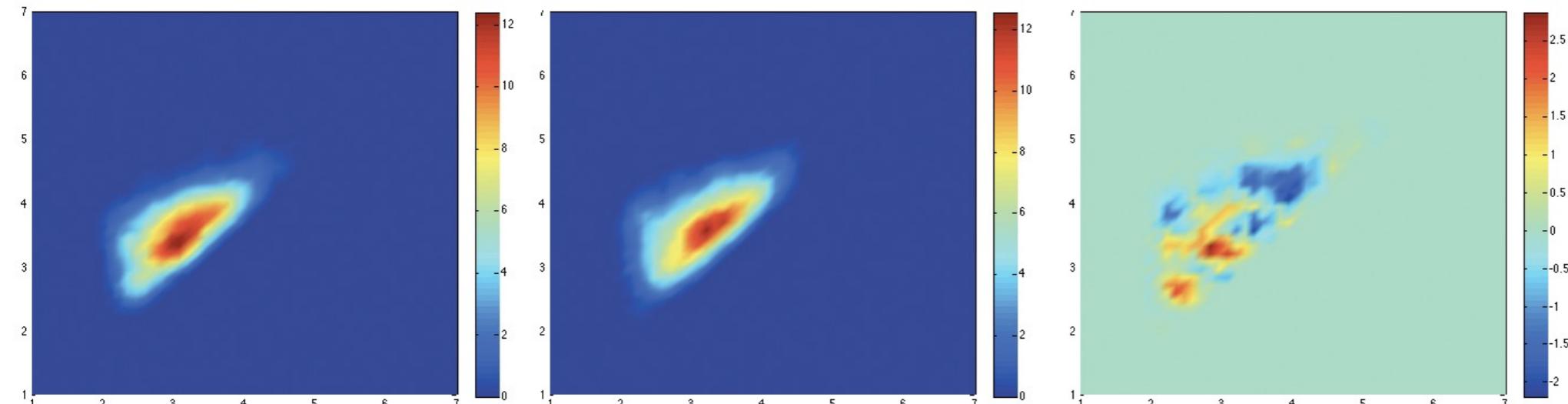
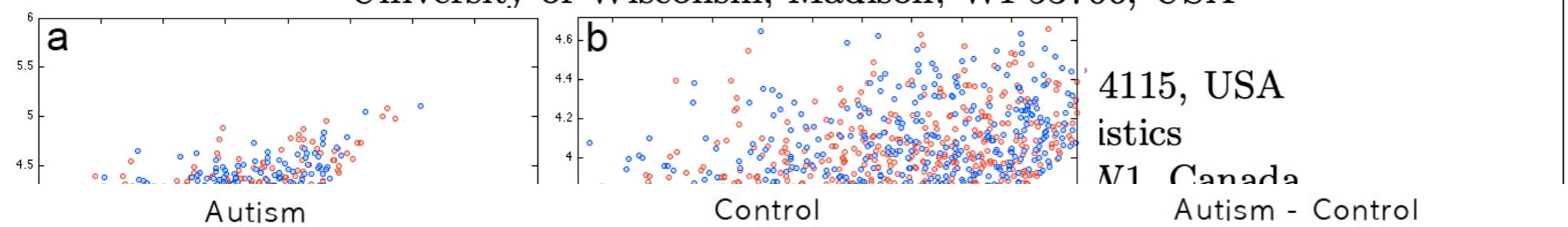
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behavior
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M1 Canada

Autism - Control



First TDA paper in
medical imaging

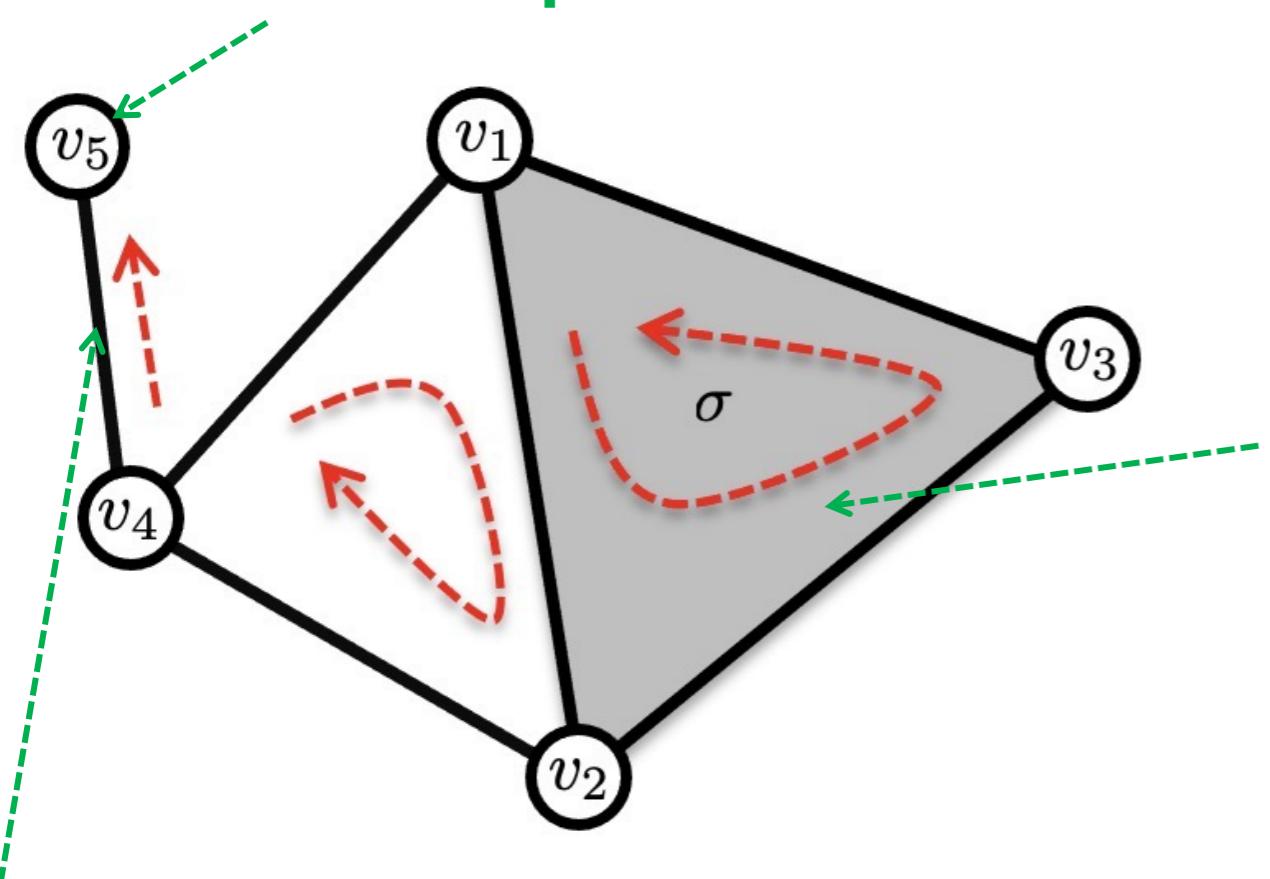
Boundary matrix

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 $[v_5]$



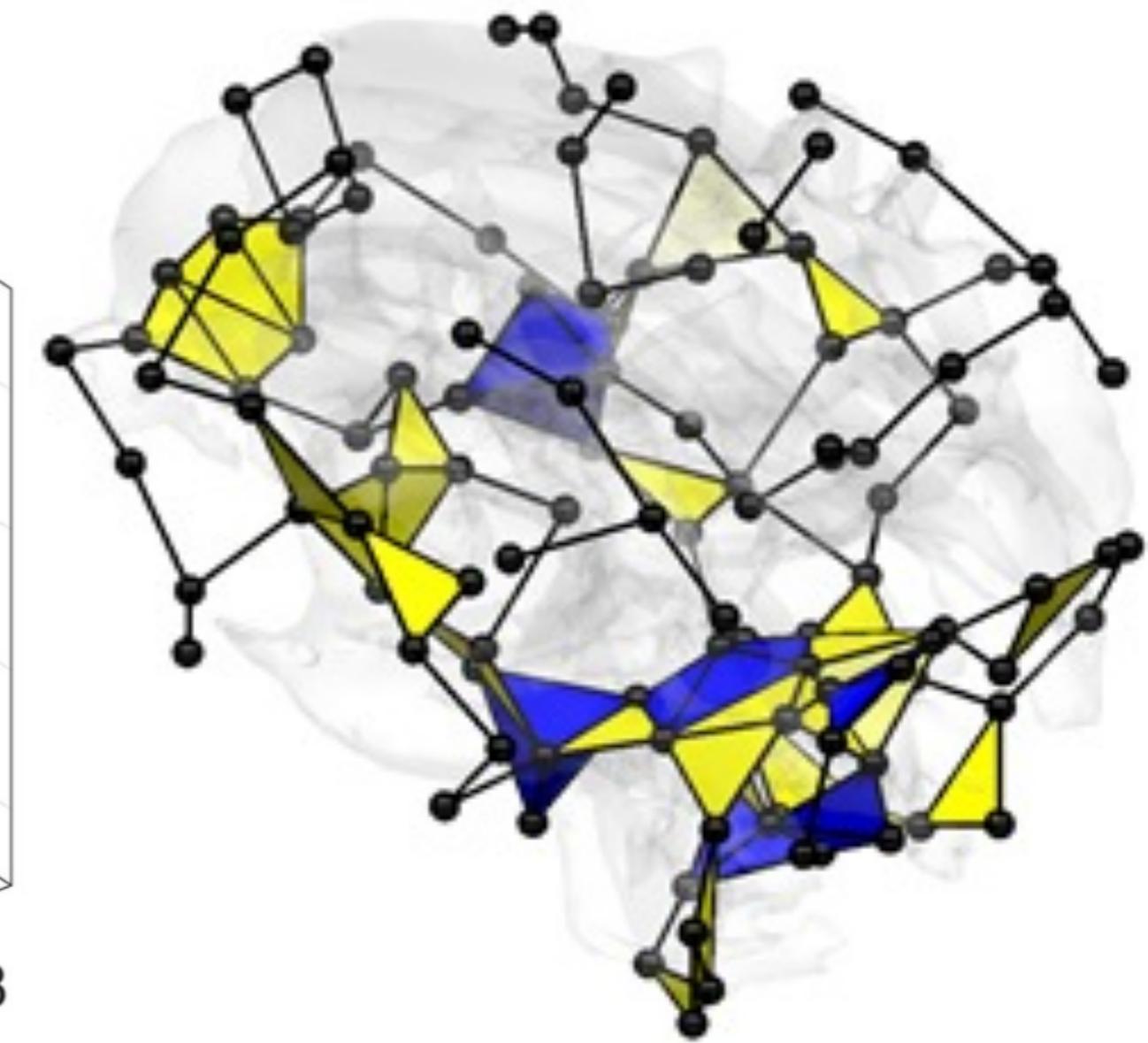
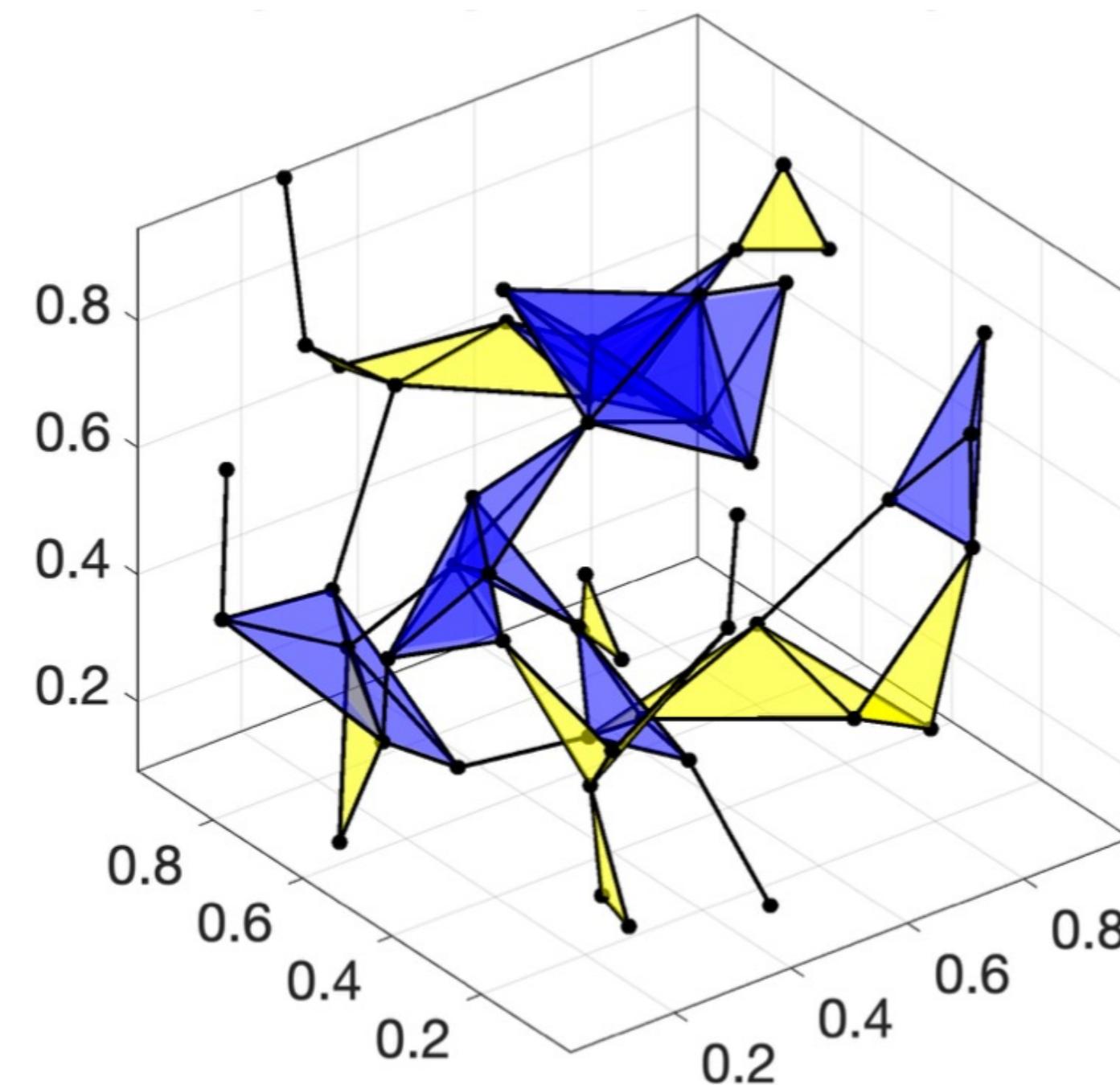
2-simplex

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

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.

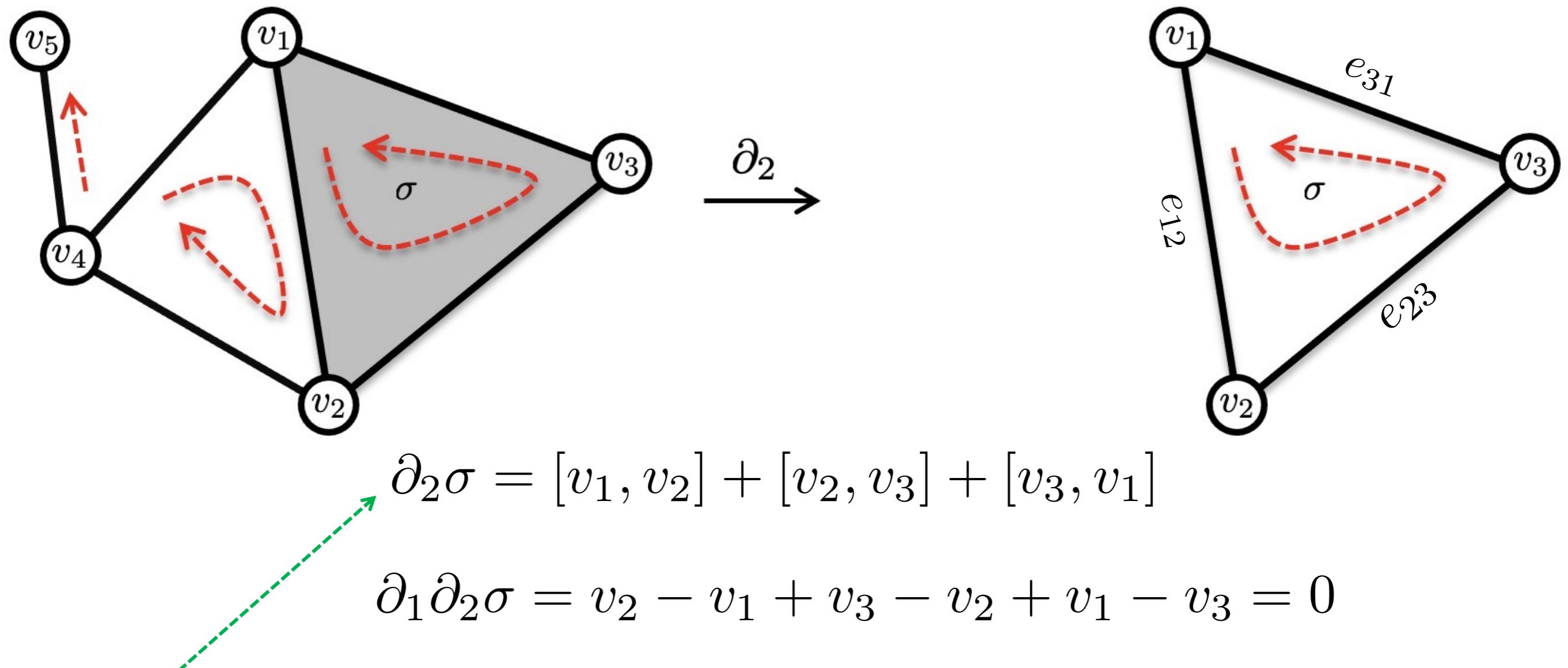


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Boundary operators ∂_k

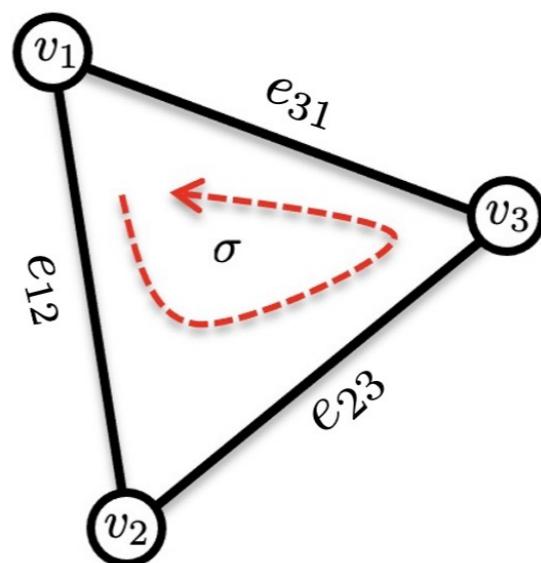
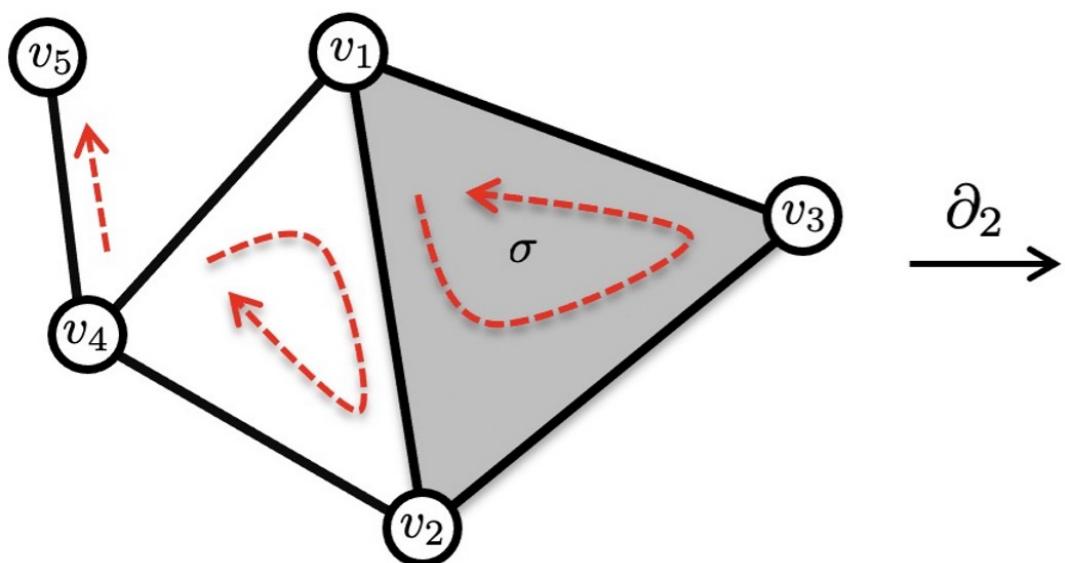
∂_k Removes the filled-in interior of k -simplexes

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



Node to edge connectivity information

Boundary matrix

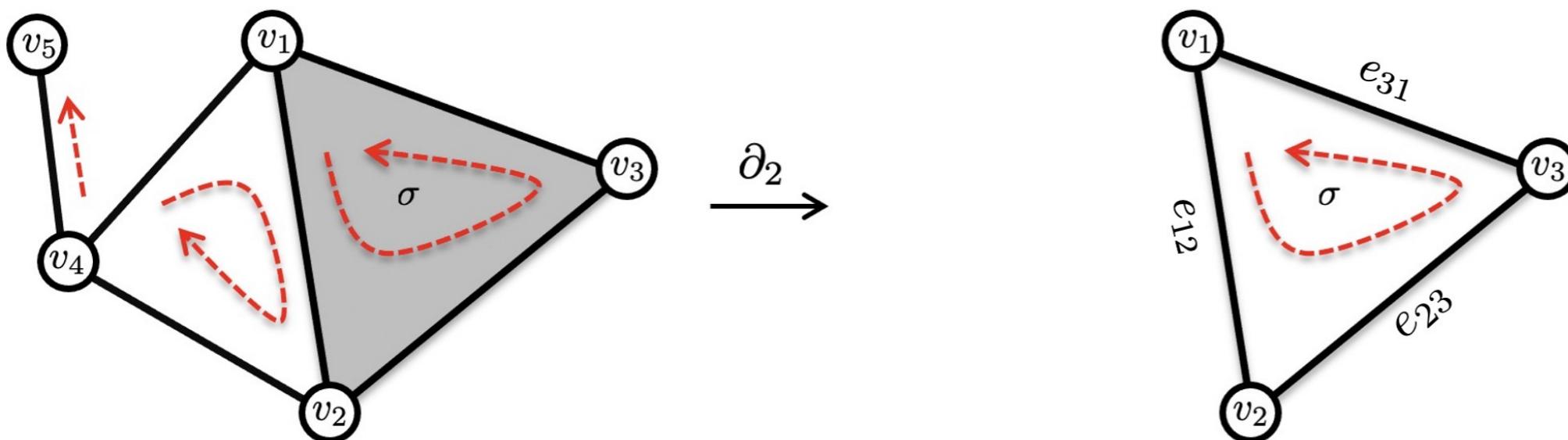
 ∂_0 

$$\partial_0 = \begin{pmatrix} v_1 & v_2 & v_3 & v_4 & v_5 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}$$

Boundary matrix

∂_1

edge to node



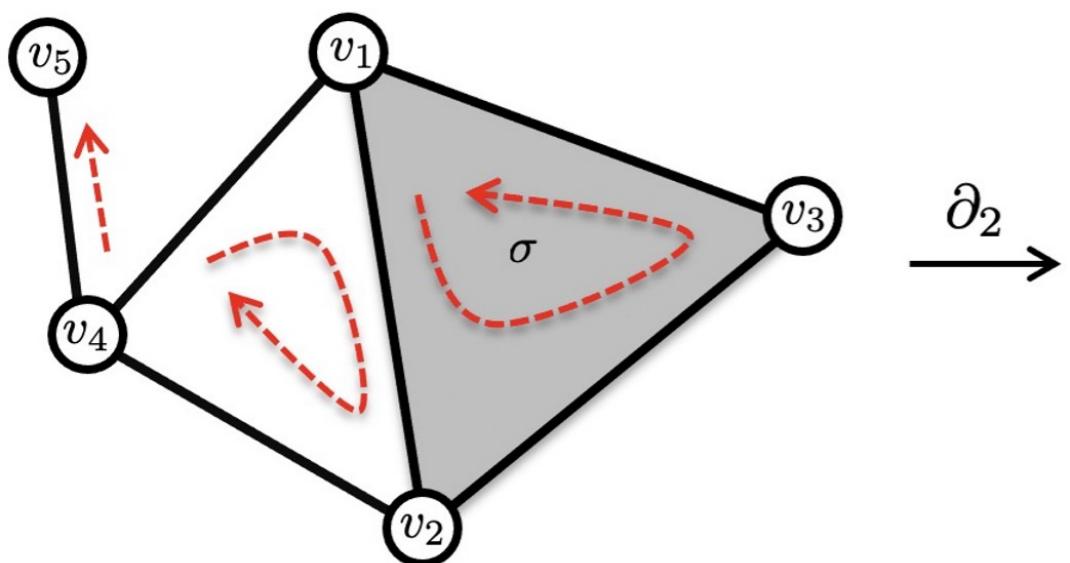
$$\partial_1 \partial_2 \sigma = v_2 - v_1 + v_3 - v_2 + v_1 - v_3 = 0$$

$$\partial_1 = \begin{matrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \end{matrix} \left(\begin{array}{cccccc} e_{12} & e_{23} & e_{31} & e_{24} & e_{41} & e_{45} \\ -1 & 0 & 1 & 0 & 1 & 0 \\ 1 & -1 & 0 & -1 & 0 & 0 \\ 0 & 1 & -1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & -1 & -1 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{array} \right)$$

Boundary matrix

∂_2

face to edge



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

$$\partial_2 = \begin{matrix} \sigma \\ e_{12} \\ e_{23} \\ e_{31} \\ e_{24} \\ e_{41} \\ e_{45} \end{matrix} = \begin{pmatrix} 1 & 1 & 1 & 0 & 0 & 0 \\ 1 & 1 & 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 0 & 1 & 0 \end{pmatrix}$$

Boundary matrix ∂_k

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

Sign depends on the orientation of τ_i

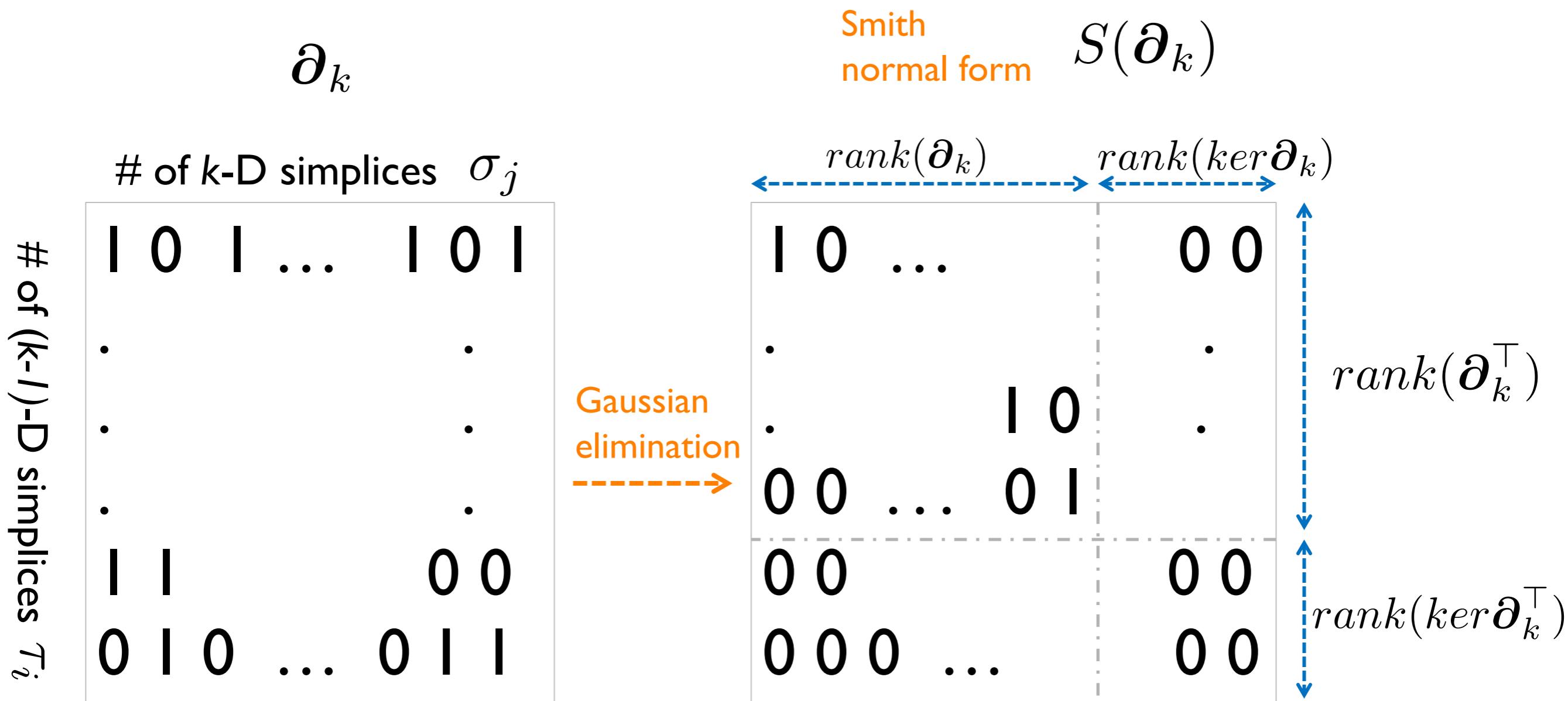
of $(k-l)$ -dimensional simplices τ_i

of k -dimensional simplices σ_j

	1	0	1	...	1	0	1
.
	1	1			0	0	
0	1	0	...	0	1	-1	

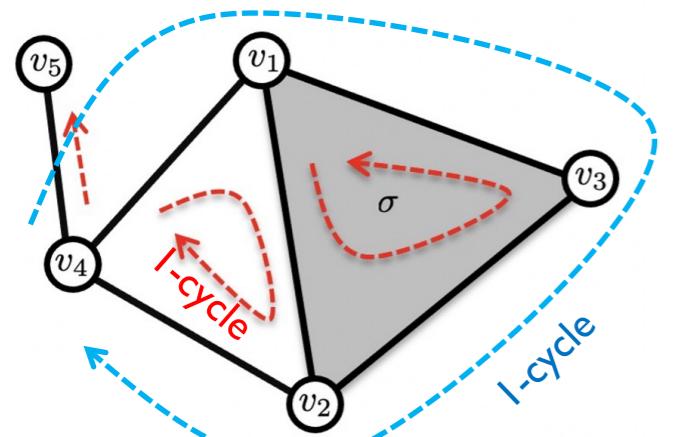
∂_k

Rank nullity theorem for boundary matrix



$$\beta_k = rank(ker\partial_k) - rank(\partial_{k+1})$$

Computing Betti numbers through boundary matrices



$$S(\partial_1) = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}, \quad S(\partial_2) = \begin{pmatrix} 1 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}$$

$$\beta_0 = \text{rank}(\ker \partial_0) - \text{rank}(\partial_1) = 5-4$$

$$\beta_1 = \text{rank}(\ker \partial_1) - \text{rank}(\partial_2) = 2-1$$

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

$$\Delta_0 = \partial_1 \partial_1^\top$$

of nodes

of nodes

1st Hodge Laplacian

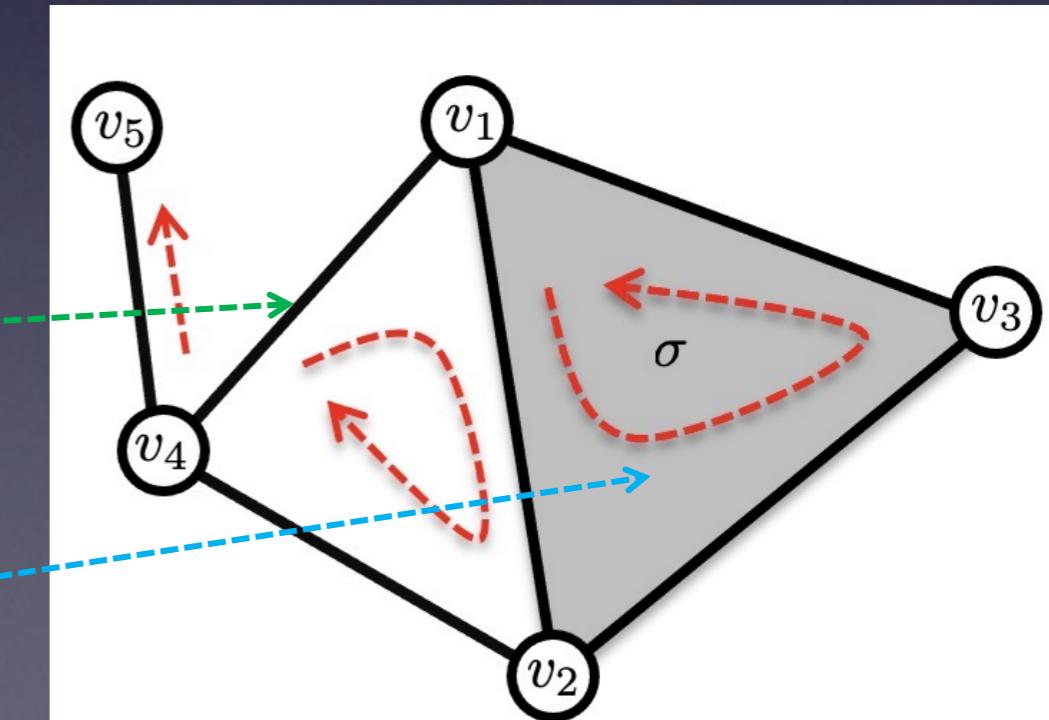
$$\Delta_1 = \partial_2 \partial_2^\top + \partial_1^\top \partial_1$$

of edges

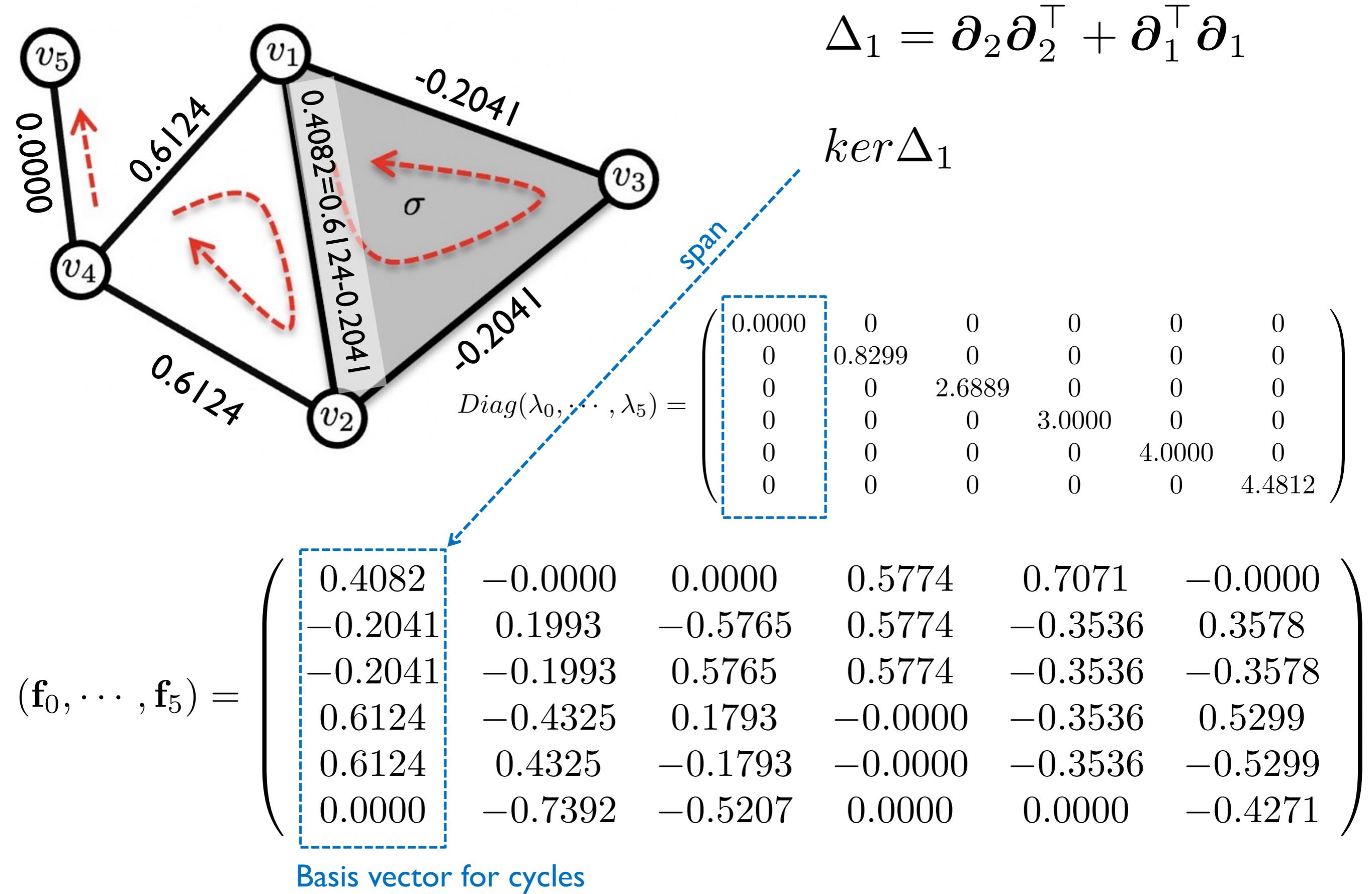
of edges

of edges

of edges

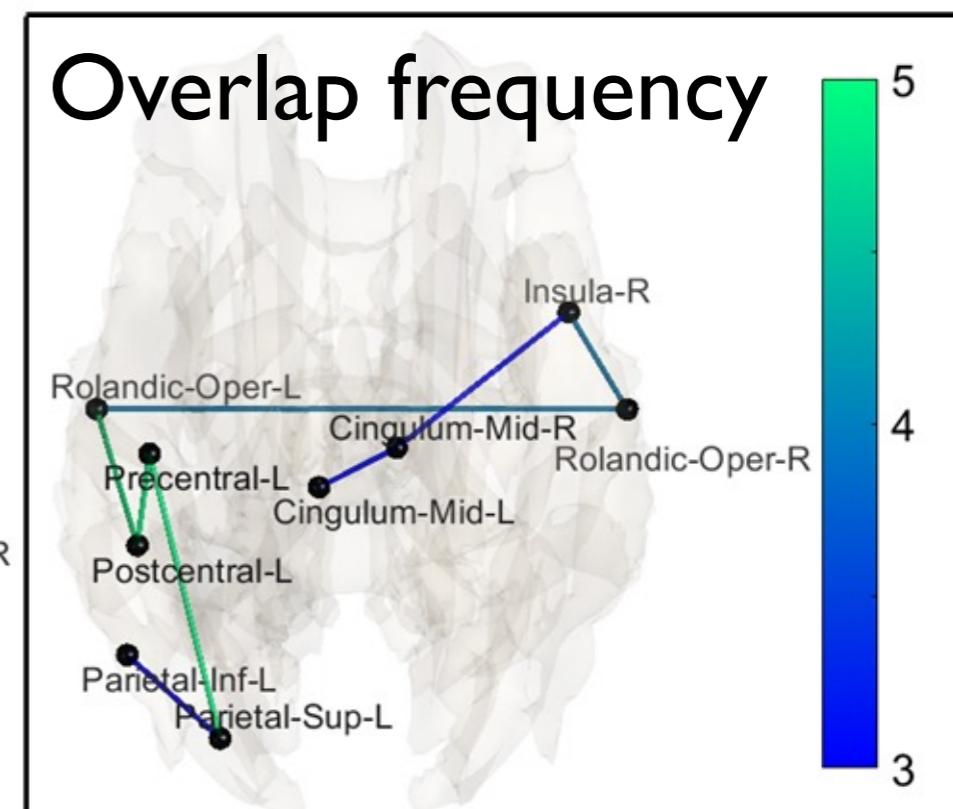
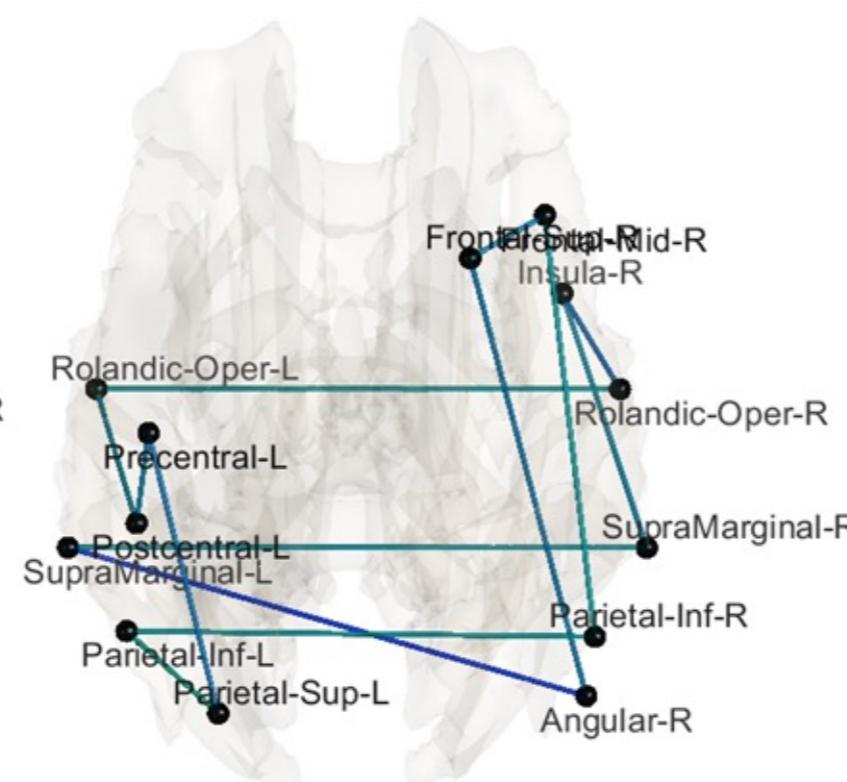
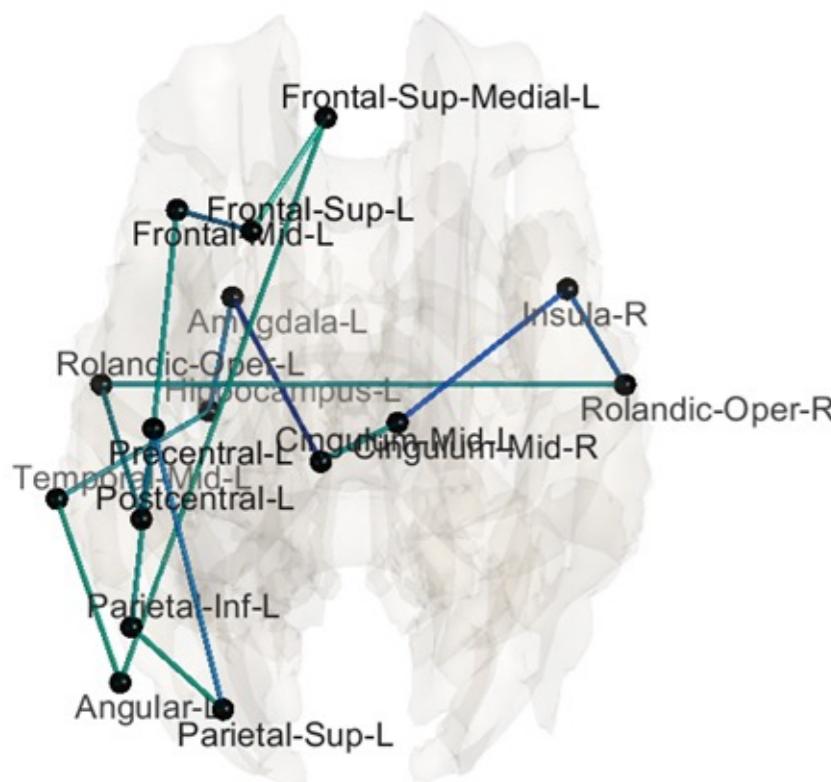
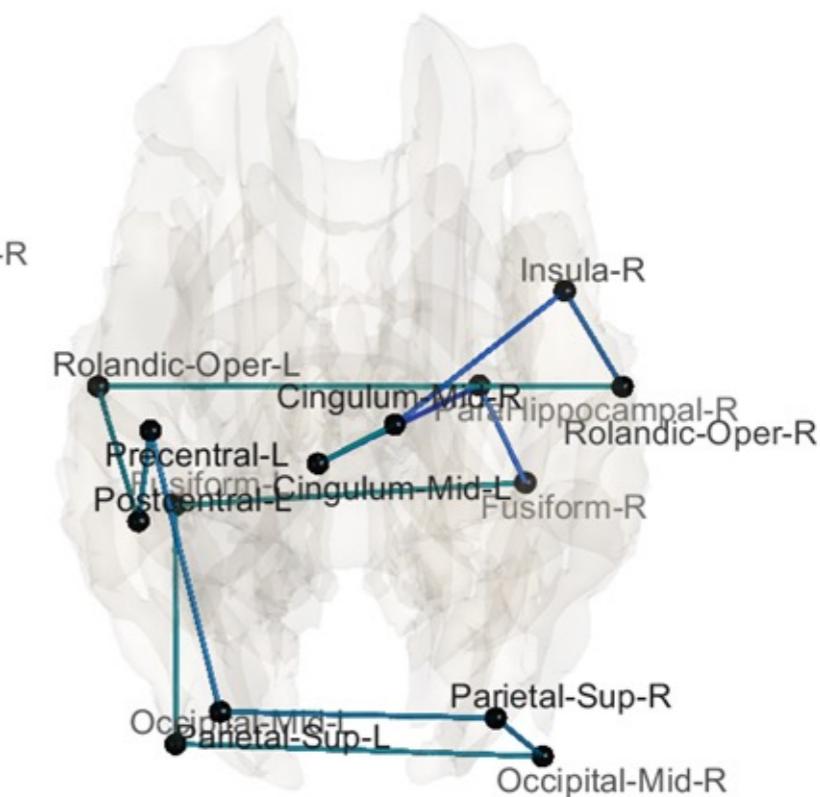
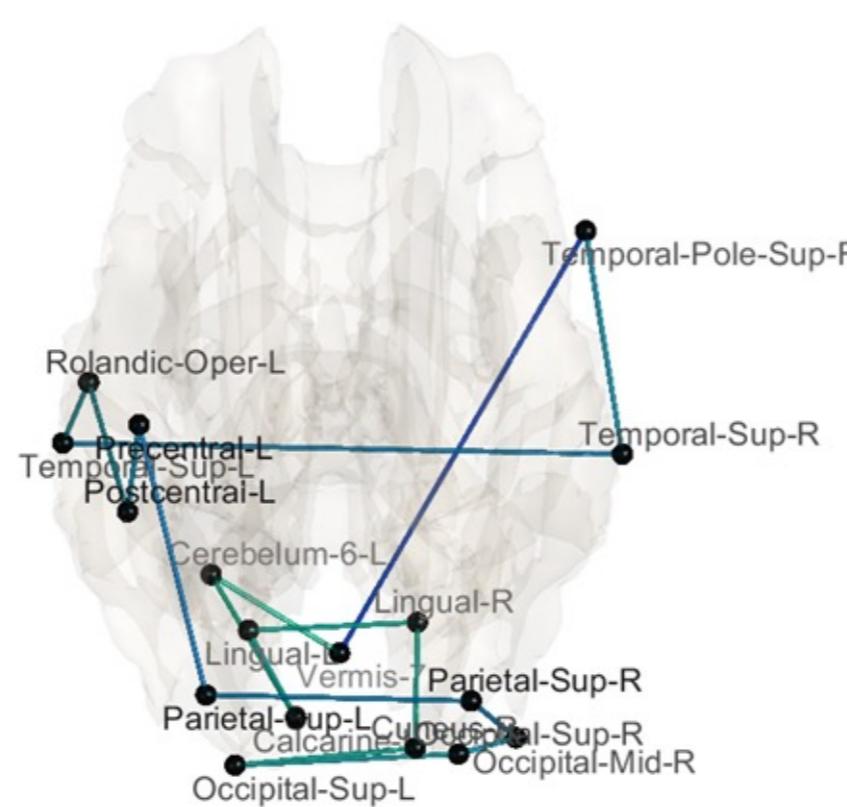
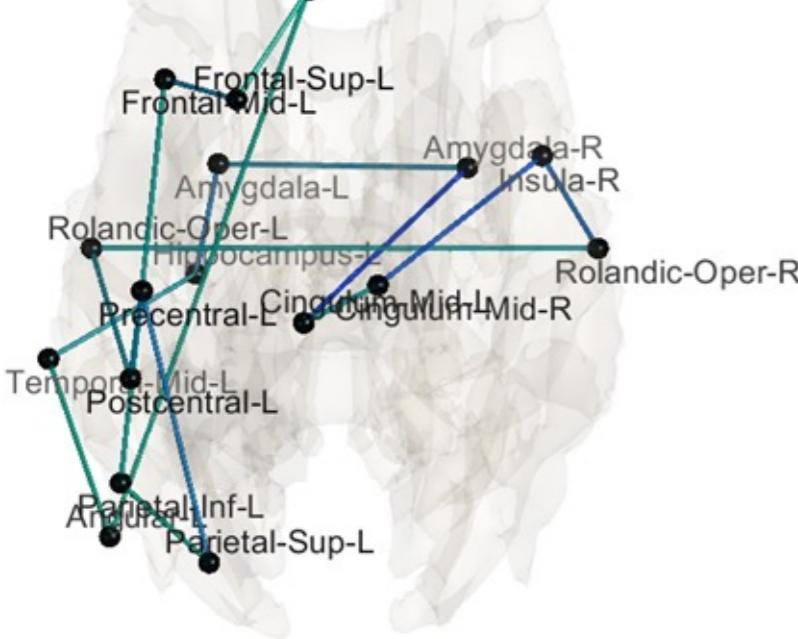


Eigenvectors of Hodge Laplacian



Five biggest cycle differences (male – female) in HCP

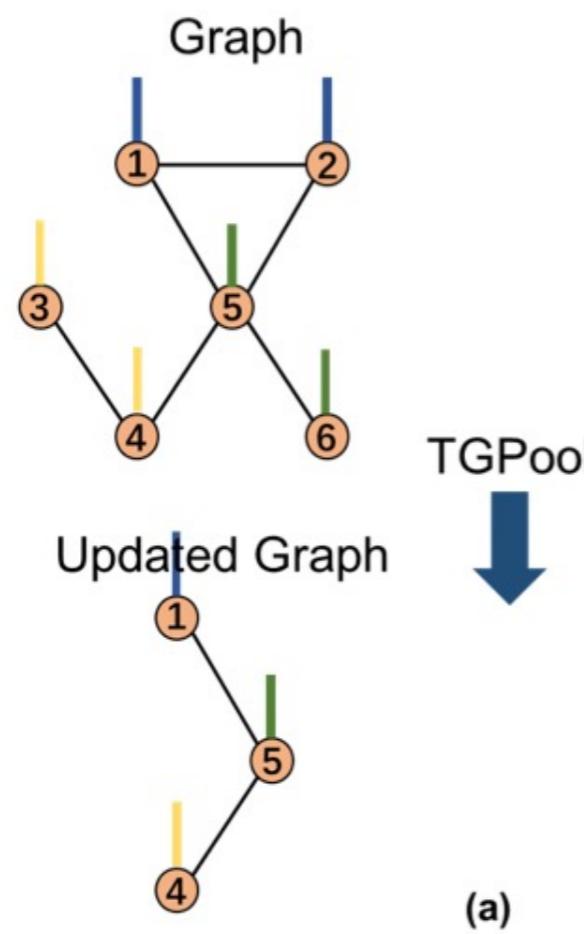
p-value = 0.03



Spectral convolution on graphs using Hodge Laplacian

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

Topological pooling



Boundary Operator ∂_1

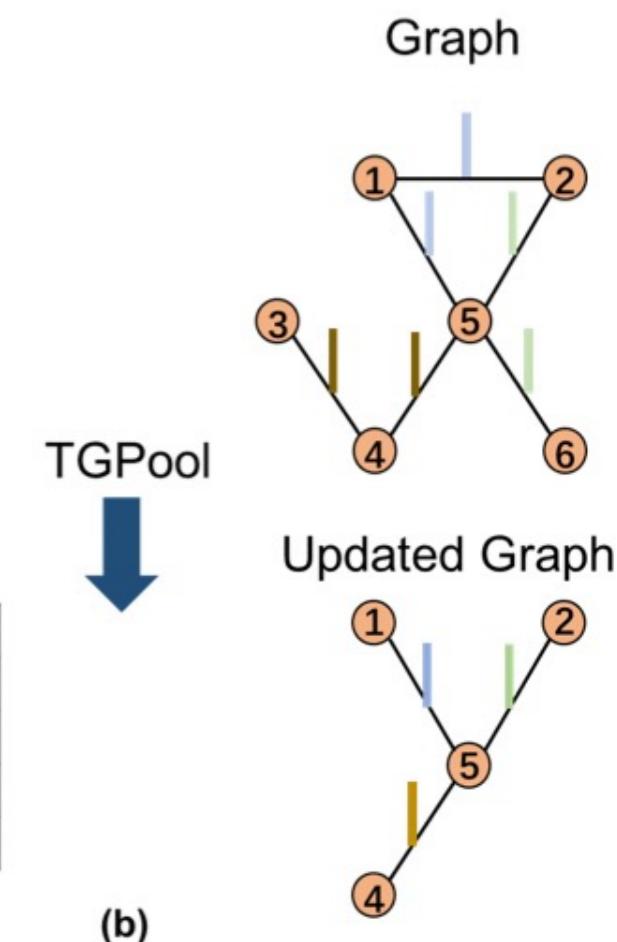
	(1, 2)	(1, 5)	(2, 5)	(3, 4)	(4, 5)	(5, 6)
1	-1	-1	0	0	0	0
2	1	0	-1	0	0	0
3	0	0	0	-1	0	0
4	0	0	0	1	-1	0
5	0	1	1	0	1	-1
6	0	0	0	0	0	1

Updated ∂_1

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

Updated ∂_1

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



Rips filtrations

Rips filtration

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Metric space

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

Node set

Metric

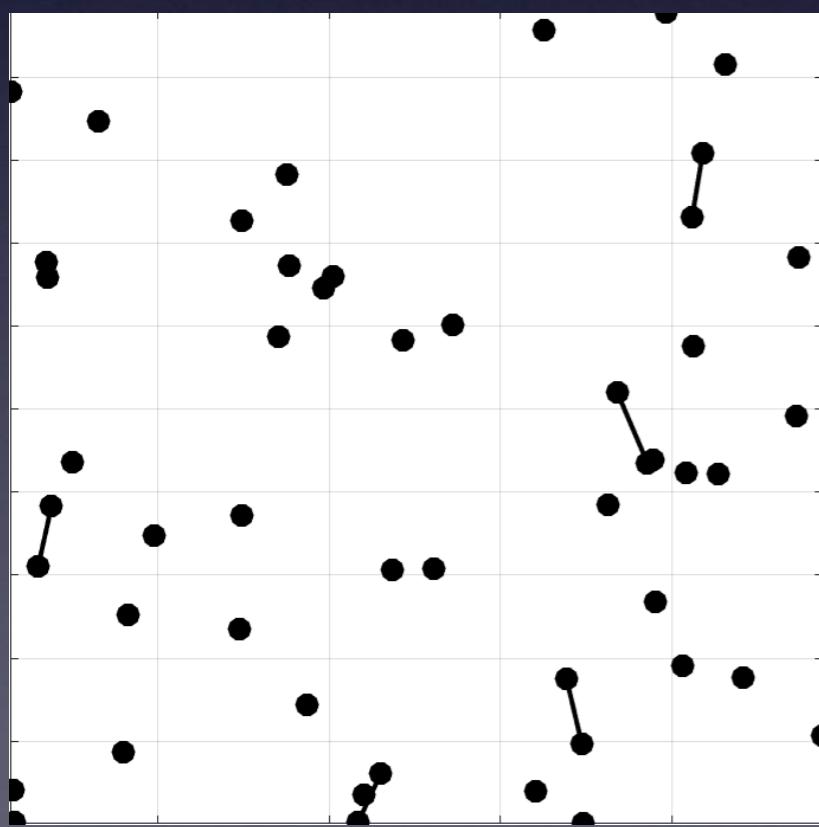
$$w_{ik} < w_{ij} + w_{jk}$$

Rips filtration

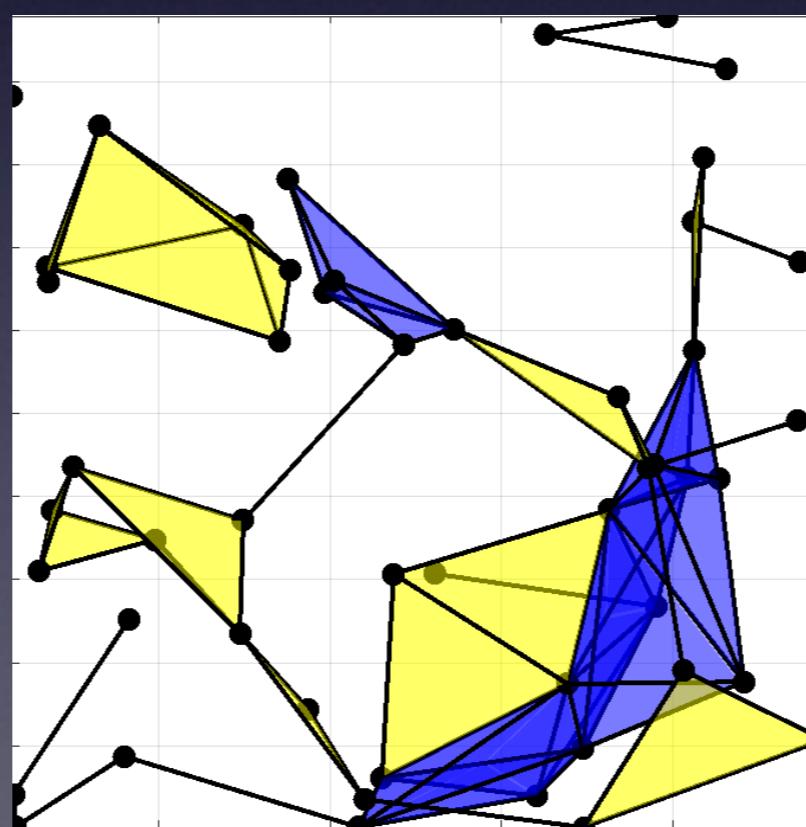
$$\mathcal{X}_{\epsilon_0} \subset \mathcal{X}_{\epsilon_1} \subset \mathcal{X}_{\epsilon_2} \subset \dots$$

for filtration values

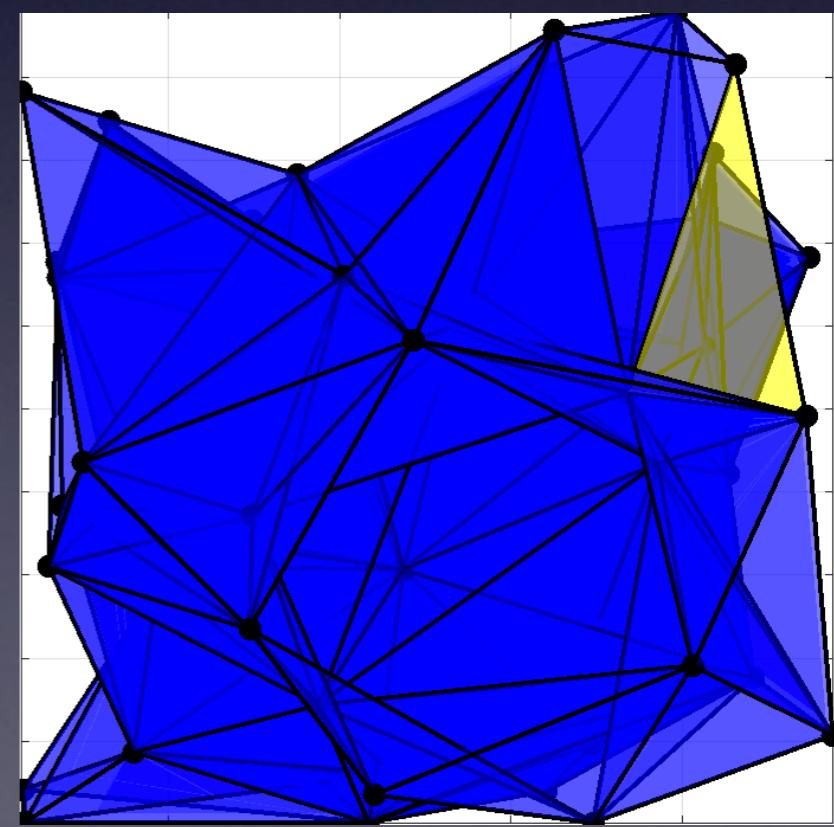
$$\epsilon_0 < \epsilon_1 < \epsilon_2 < \dots$$



$$\epsilon = 0.1$$



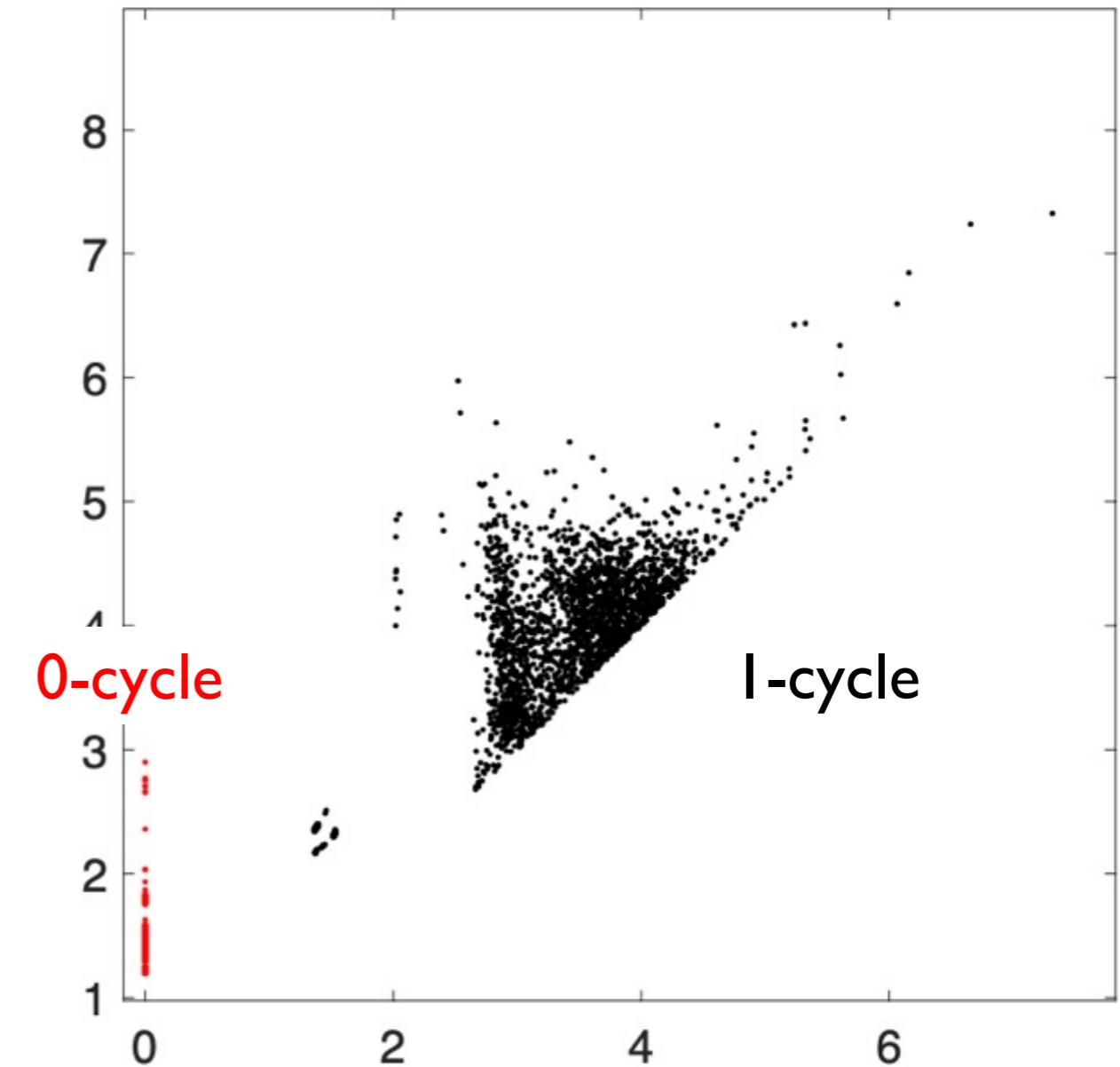
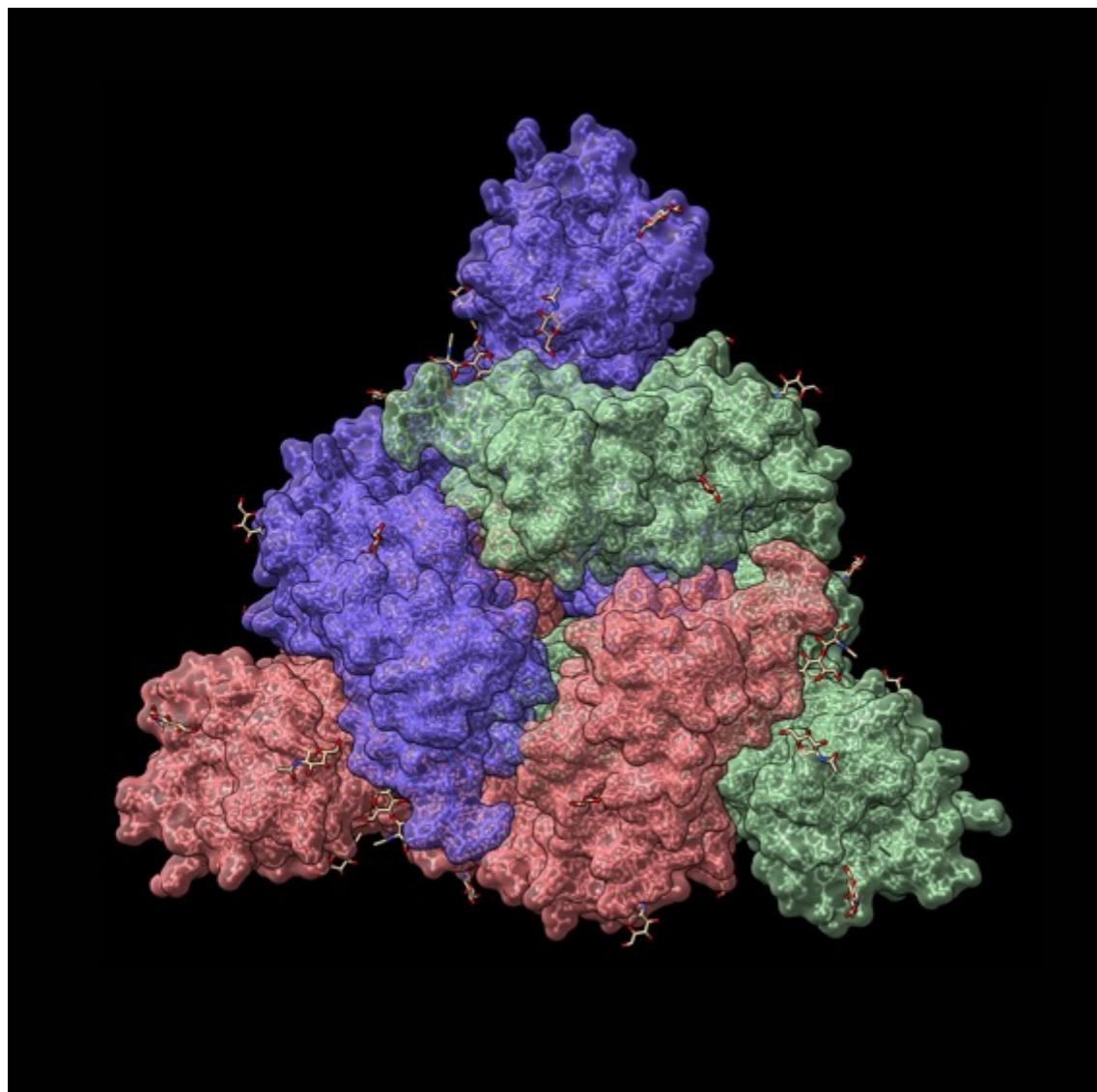
$$\epsilon = 0.3$$



$$\epsilon = 0.5$$

Persistence Diagram (PD) of a protein molecule

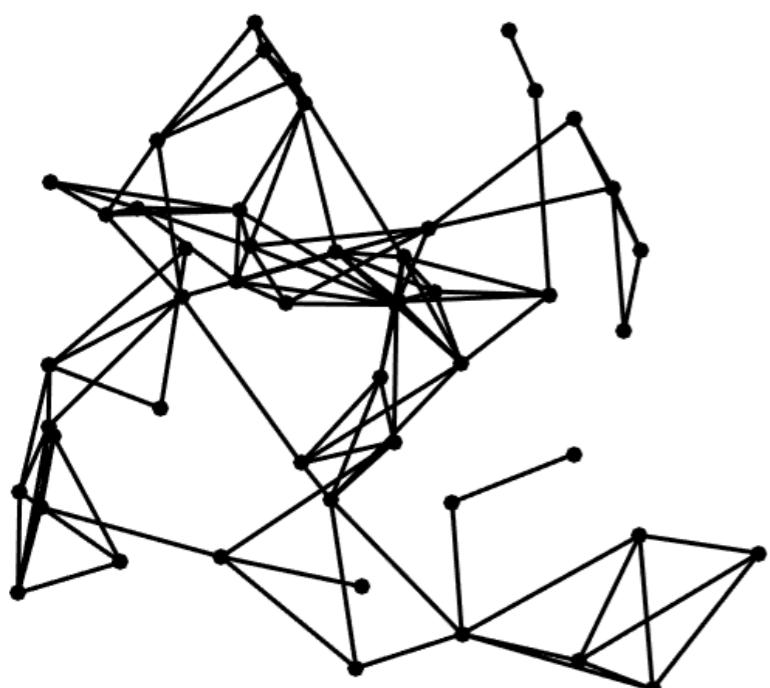
Rips filtration on distance between 8000 atoms



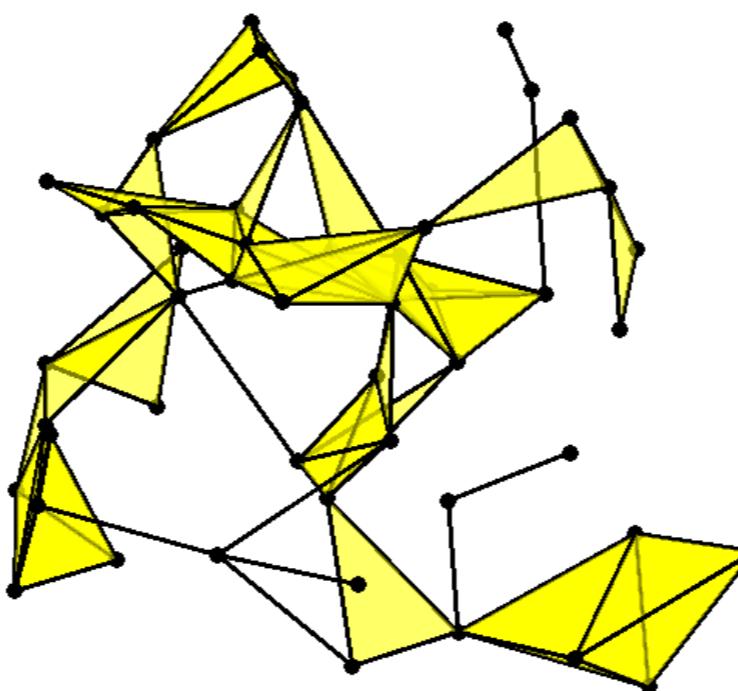
Extremely slow computation → Simply use graph filtration

k -skeleton

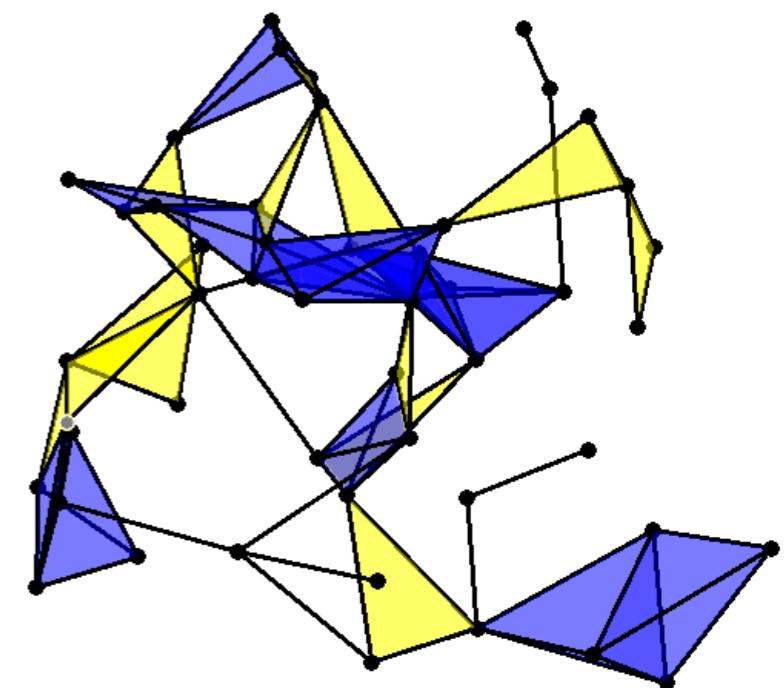
A simplicial complex consisting of up to k -simplices



1-skeleton



2-skeleton



3-skeleton

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.

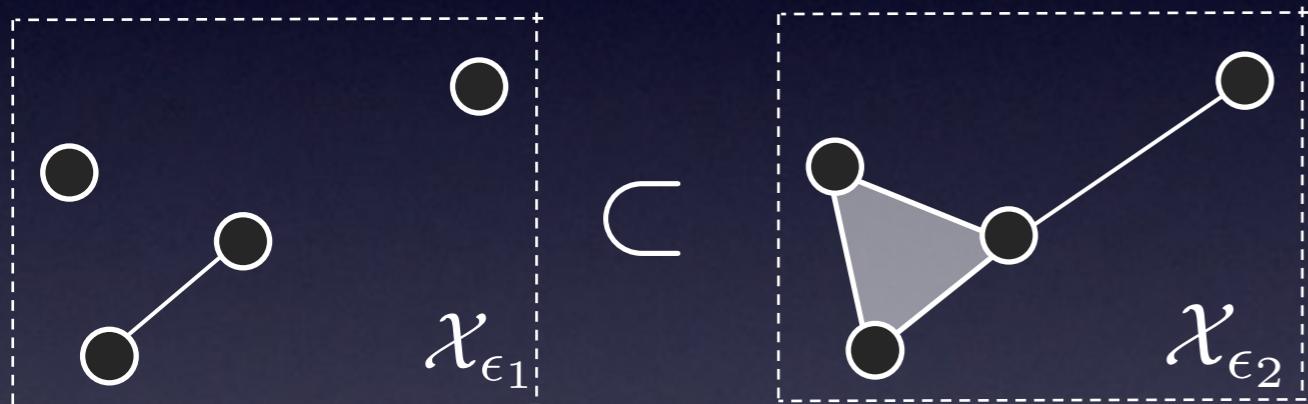
graph filtration

Metric space

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

Node set Metric

Rips complex = Simplicial complex



Rips filtration

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

for increased radius

$$\epsilon_0 < \epsilon_1 < \epsilon_2 < \dots$$

Weighted graph

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

Node set Edge weight

Binary graph: 1-skeleton



Graph filtration

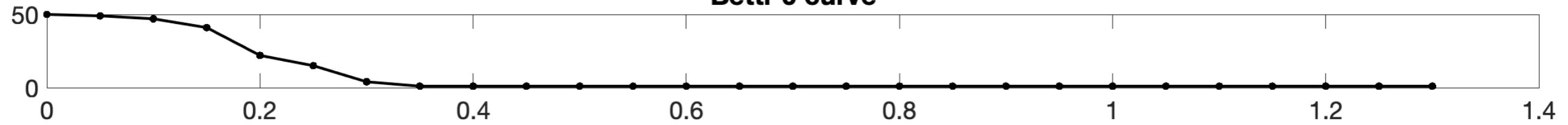
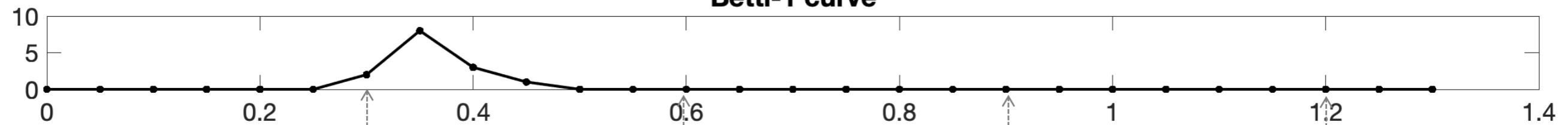
$$\mathcal{X}_{\epsilon_0} \supset \mathcal{X}_{\epsilon_1} \supset \mathcal{X}_{\epsilon_2} \supset \dots$$

for increased edge weights

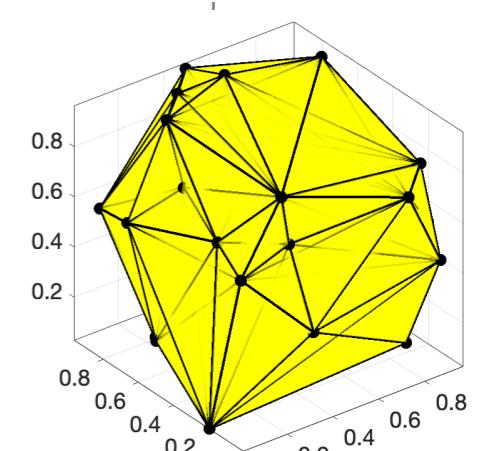
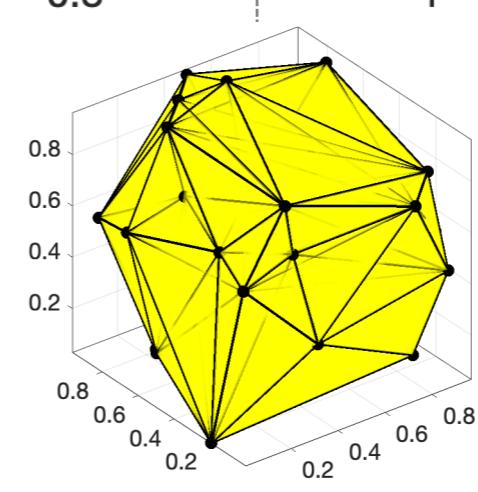
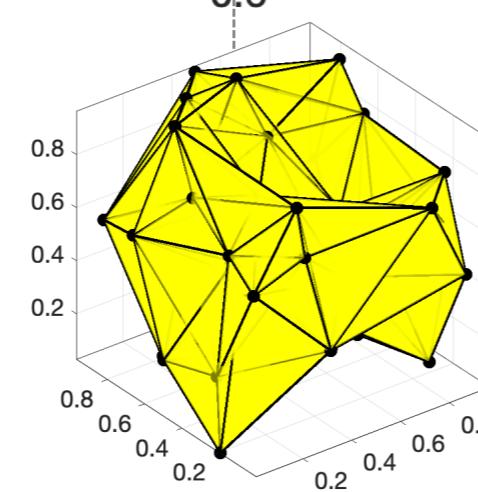
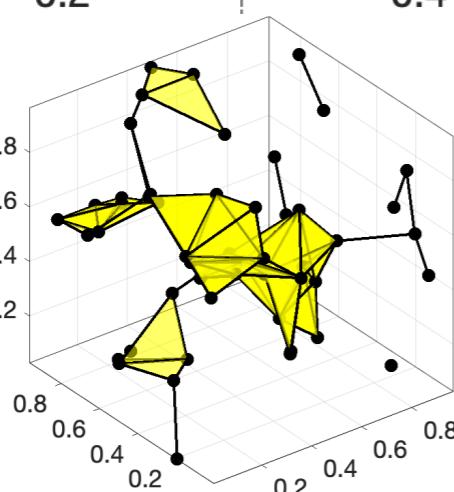
$$\epsilon_0 < \epsilon_1 < \epsilon_2 < \dots$$

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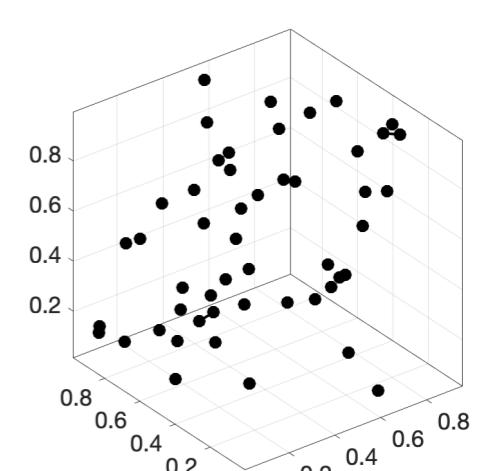
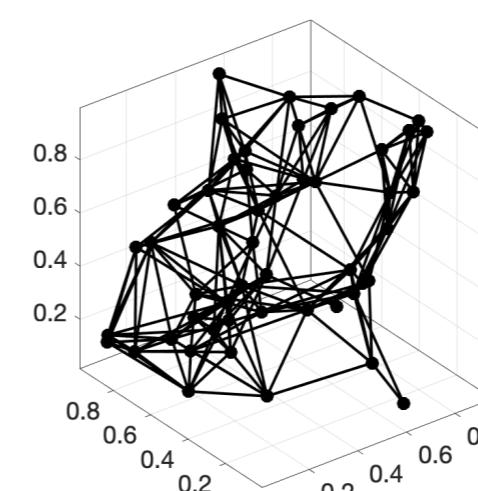
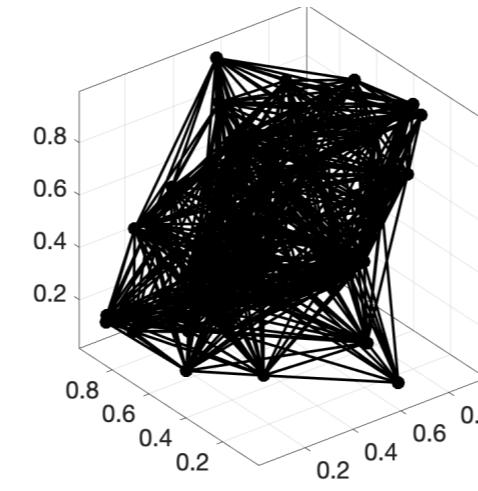
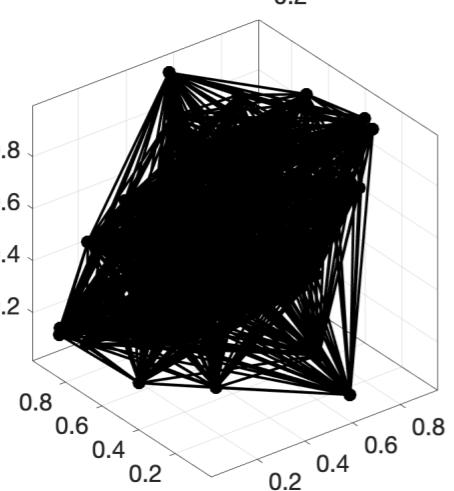
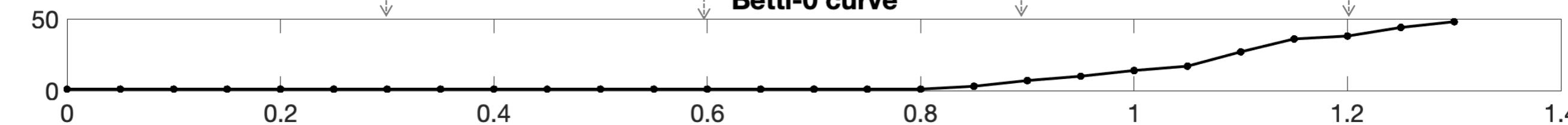
PH_graph.m

Betti-0 curve**Betti-1 curve**

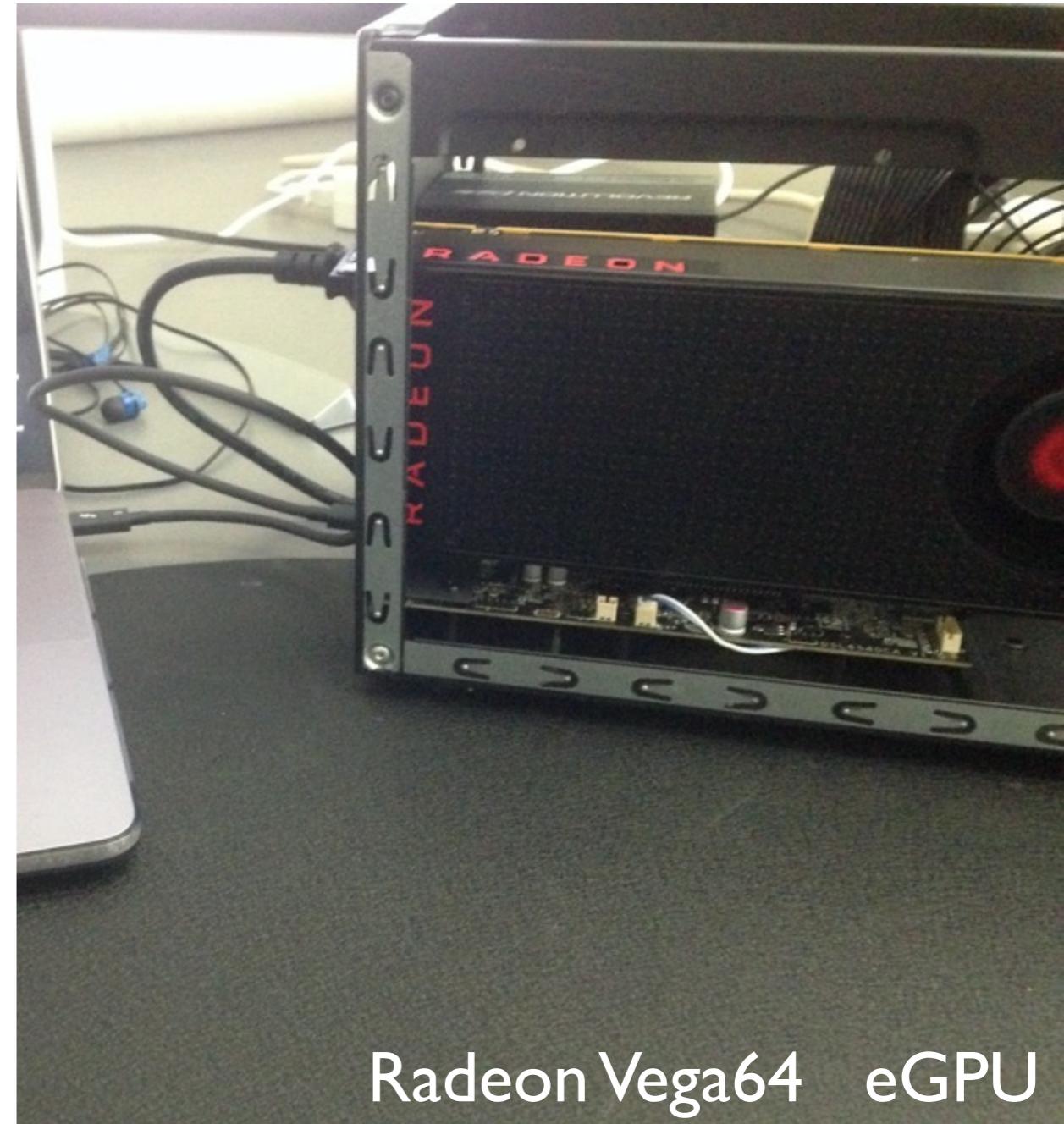
Rips
filtration



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?

Fast computation of Betti curves

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

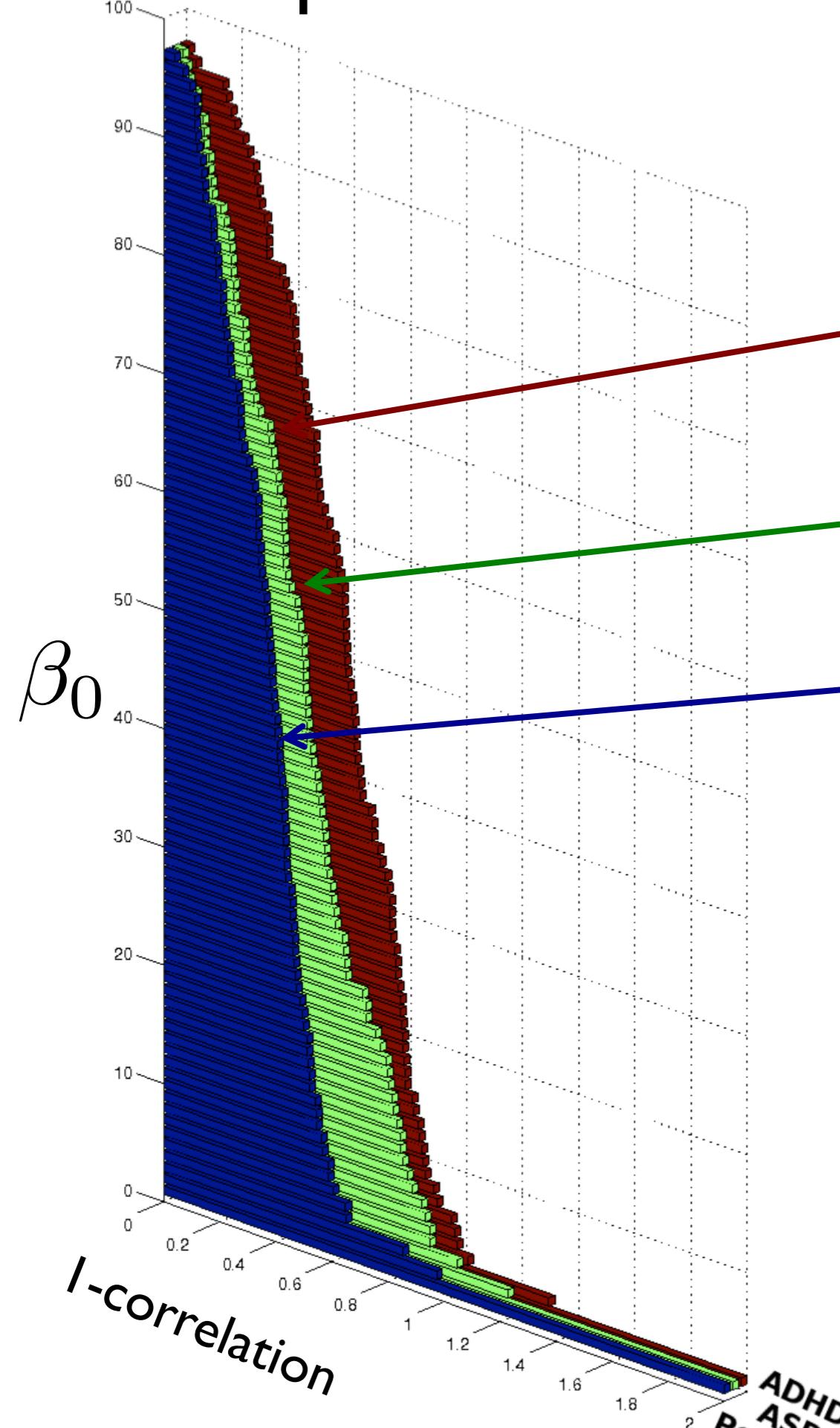
```
[beta_0, S] = graphconncomp(adj)
```

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;
```

0-th Betti plot on PET correlation network

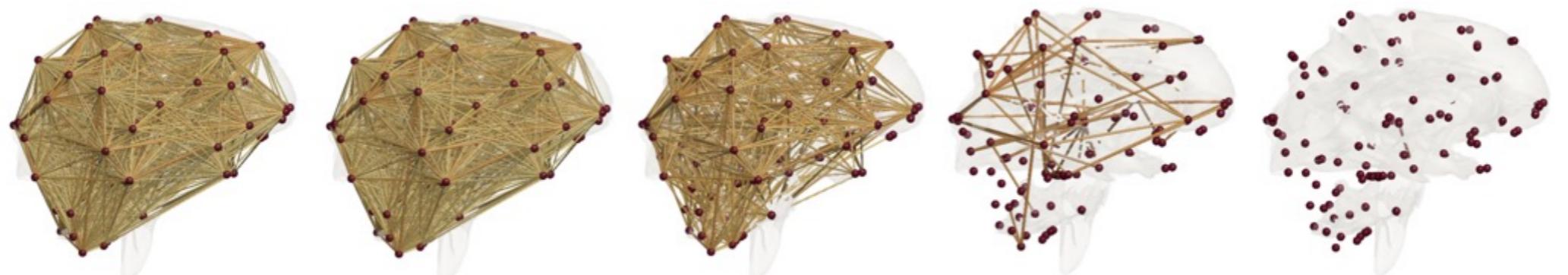


24 attention deficit hyperactivity disorder (ADHD) children
26 autism spectrum disorder (ASD) children
11 pediatric control subjects

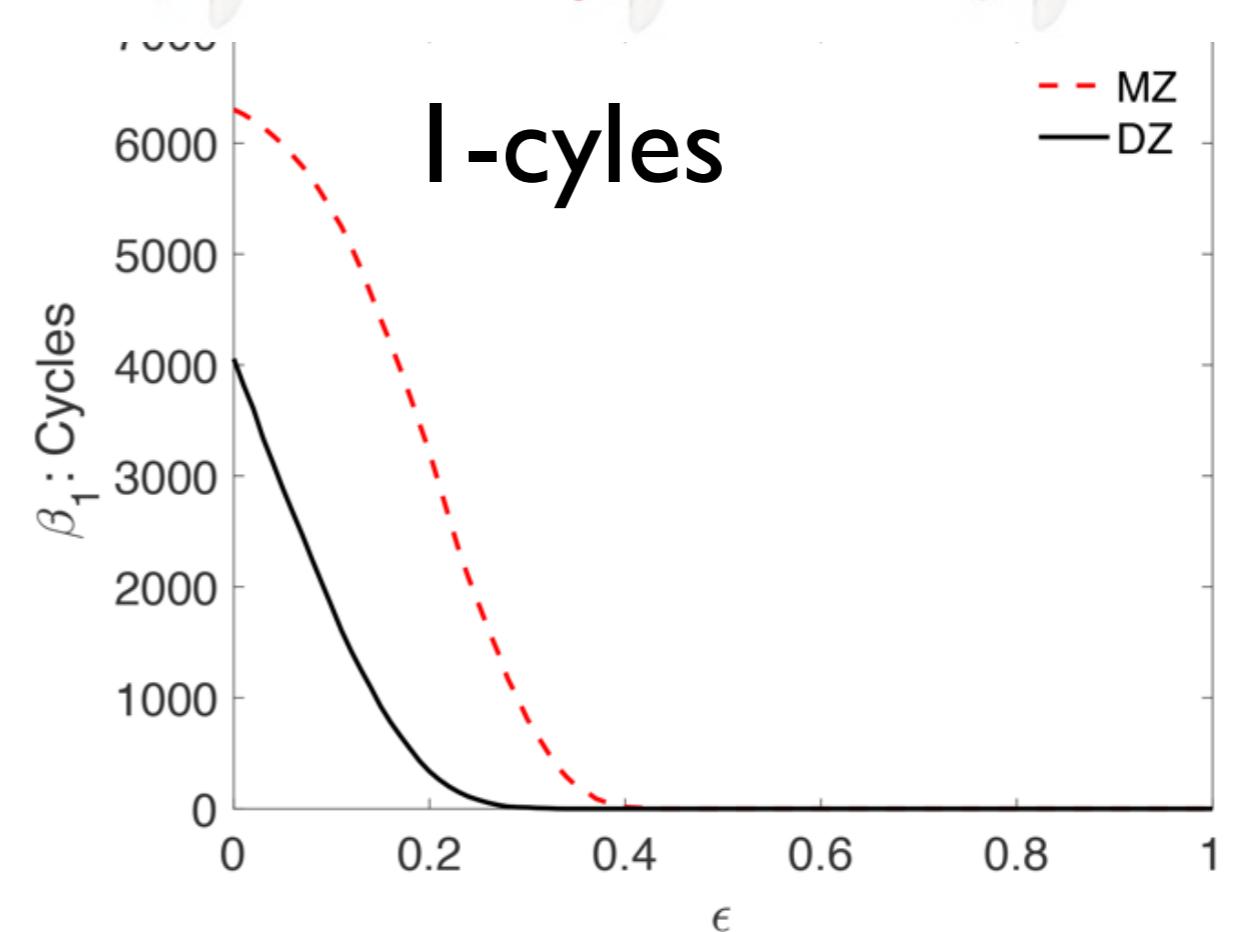
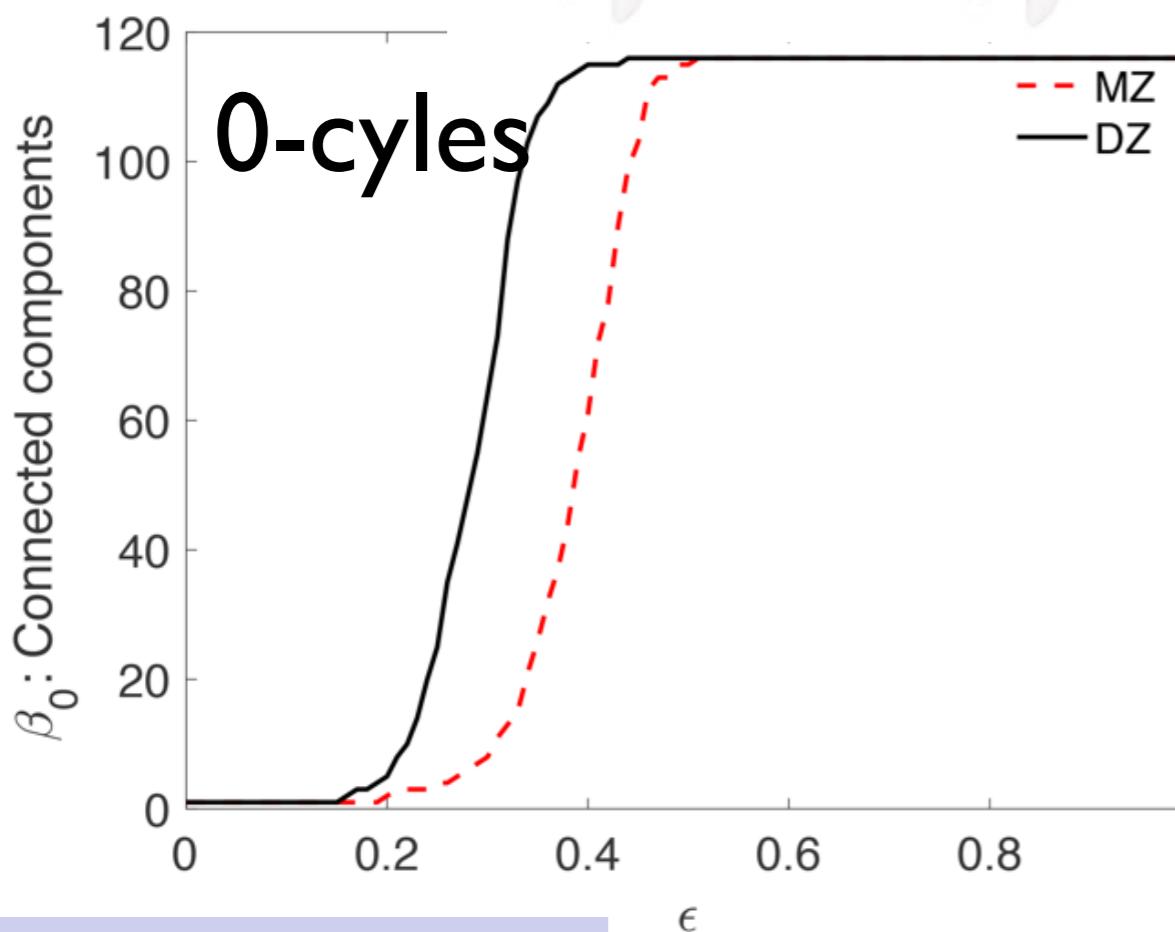
PH_betti.m

Genetic effect on Betti curves of rs-fMRI network

MZ-twins



DZ-twins



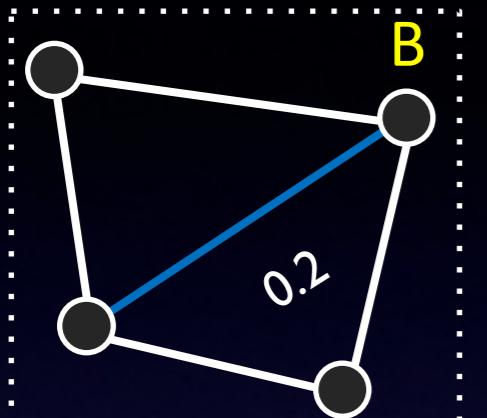
Birth and death decomposition

Songdechakraiwut et al. 2021 MICCAI 166-176

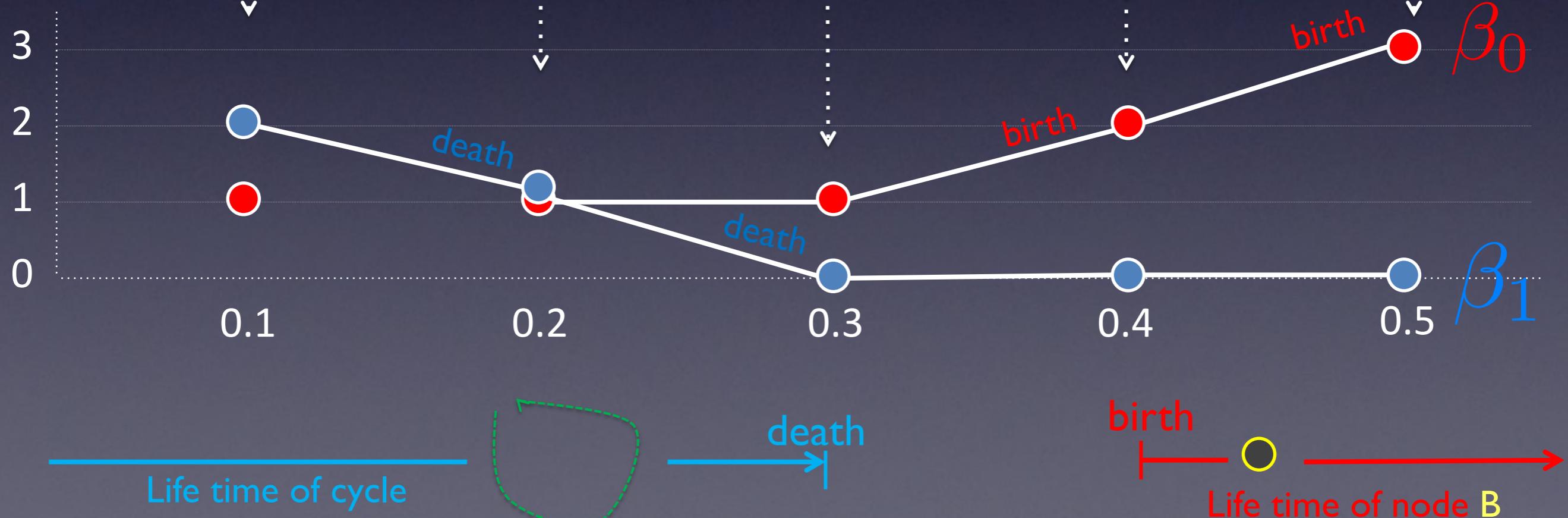
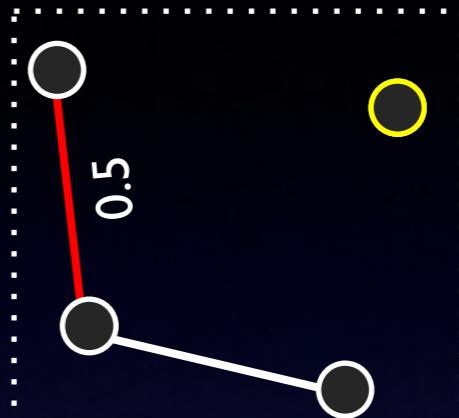
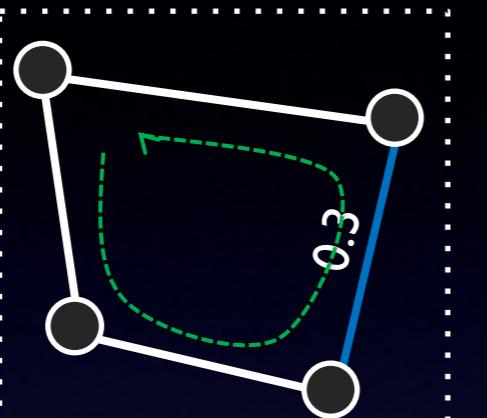
Songdechakraiwut and Chung. 2023, Annals of Applied Statistics

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

Edges destroy cycles

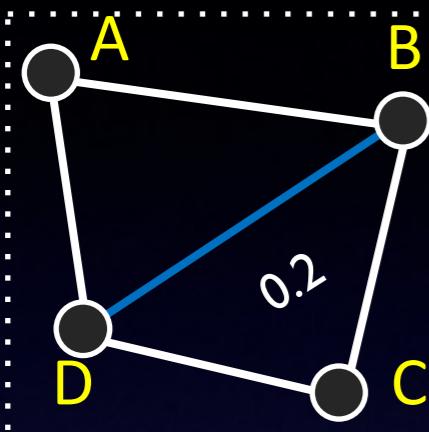


Edges create components

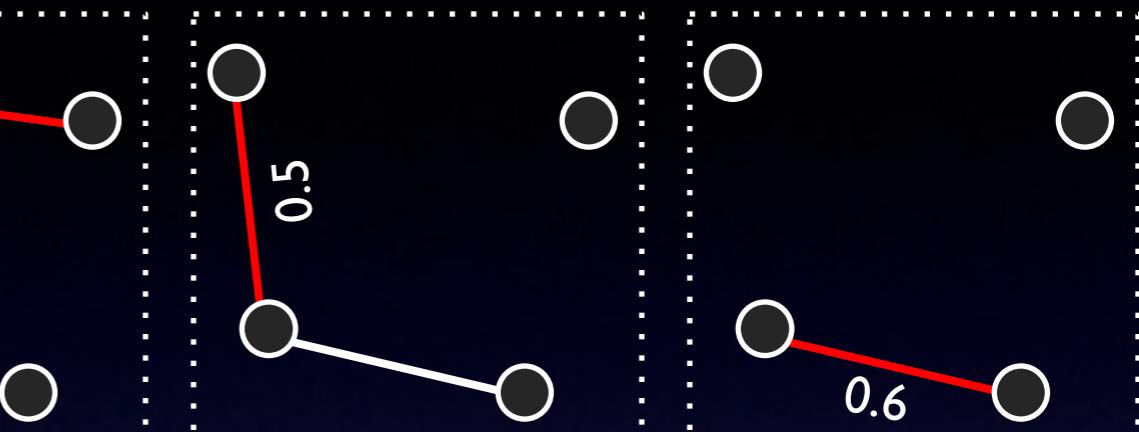
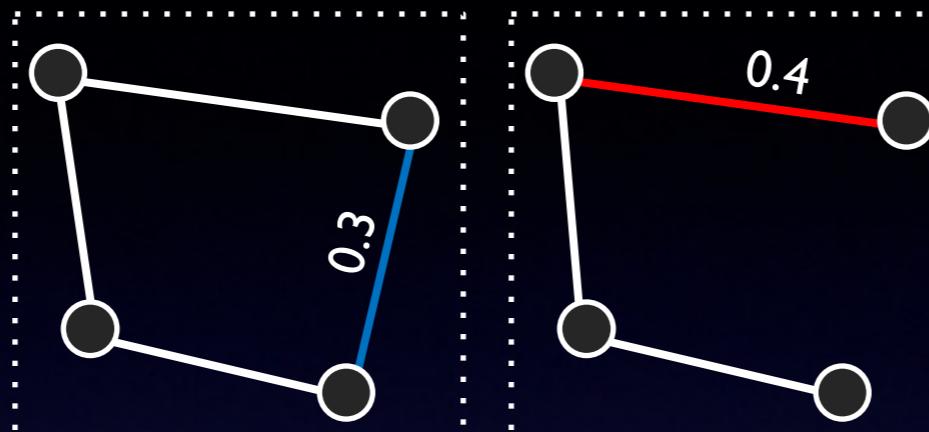


Theorem Birth & death sets partition the edge set

E_1 Edges destroy cycles



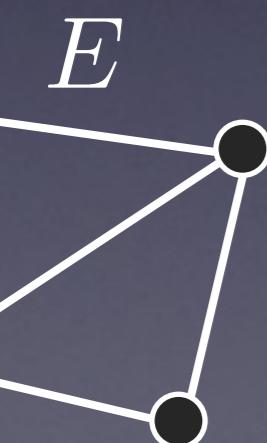
E_0 Edges create components



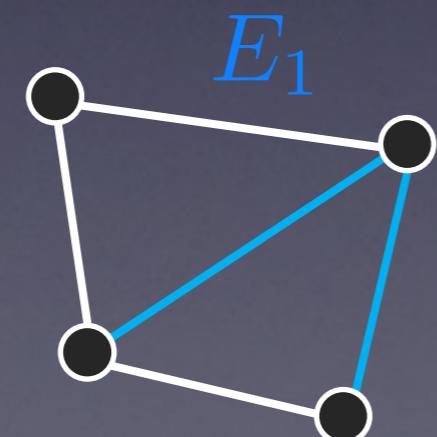
$$\#(E_1) = 1 + \frac{|V|(|V| - 3)}{2}$$

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

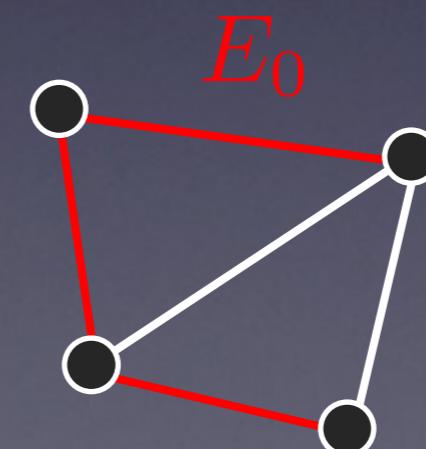
$$\#(E_0) = |V| - 1$$



=

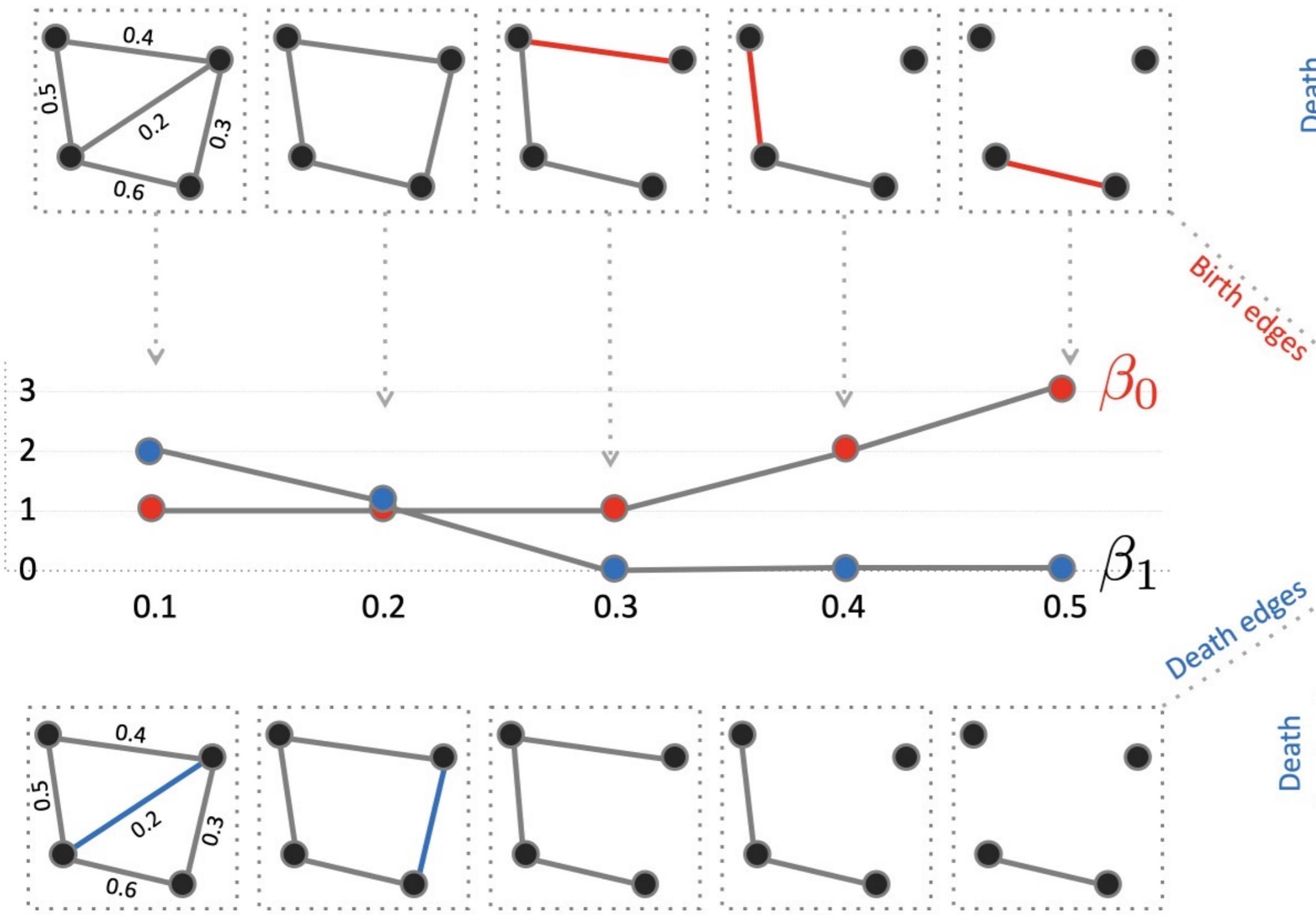


\cup



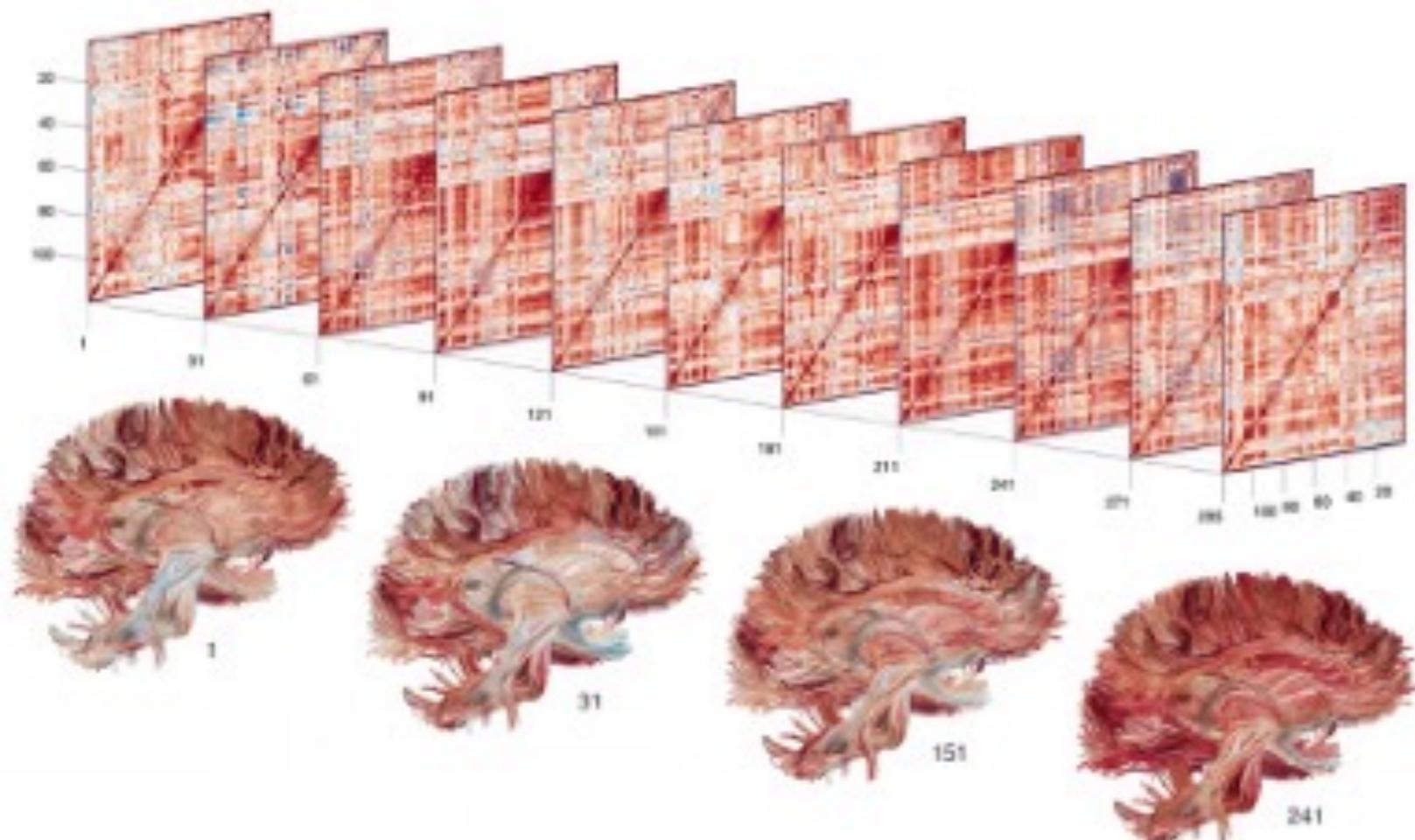
Maximum
spanning
tree

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

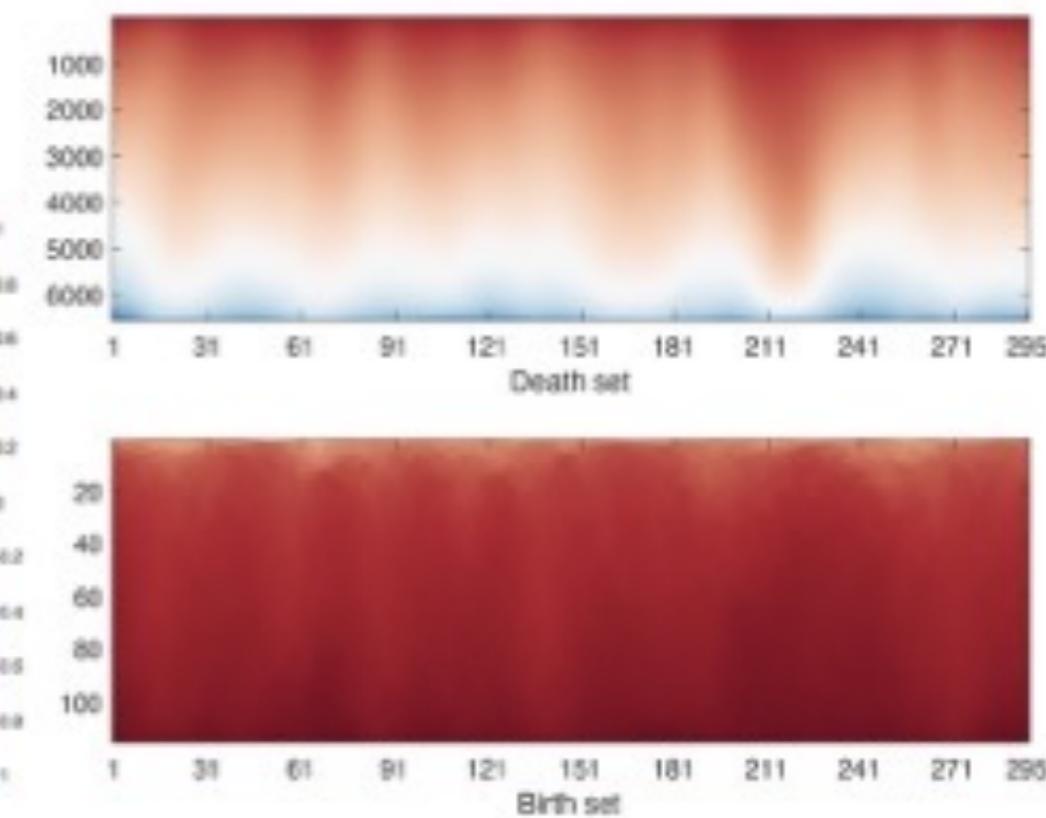


WS_decompose.m

Dynamically changing correlation network from rs-fMRI



Dynamically changing birth-death sets



WS_decompose.m

Topological inference

Songdechakraiwut and Chung. 2023, Annals of
Applied 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: $\mathcal{D}(X, Y) = (\inf \mathbb{E} \|X - Y\|^2)^{1/2}$

Persistent diagrams

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

Empirical distributions

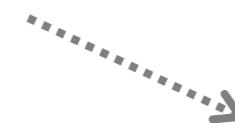
$$f_1(x) = \frac{1}{q} \sum_{i=1}^q \delta(x - x_i)$$

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

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

Assignment problem: Hungarian algorithm

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

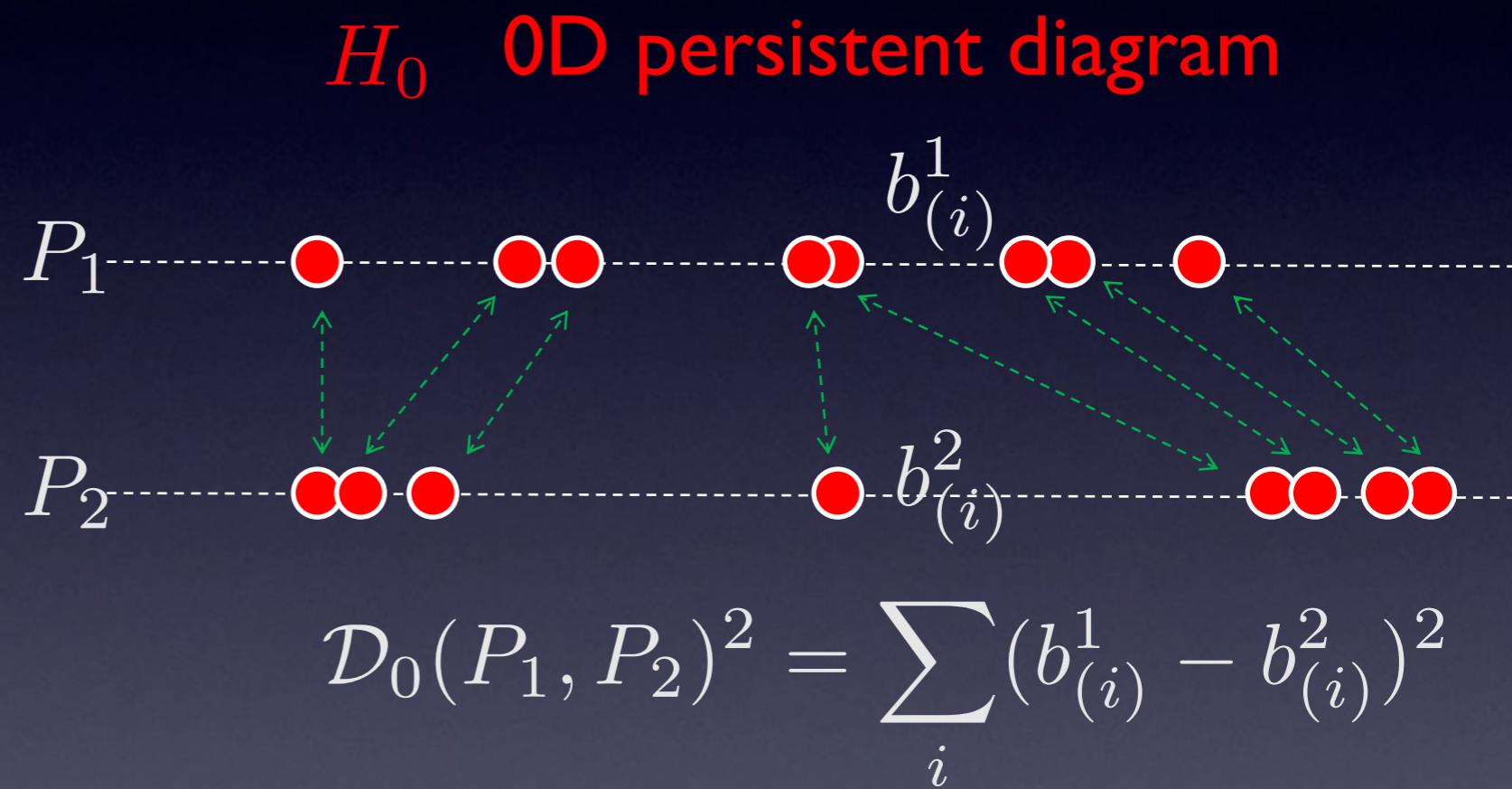
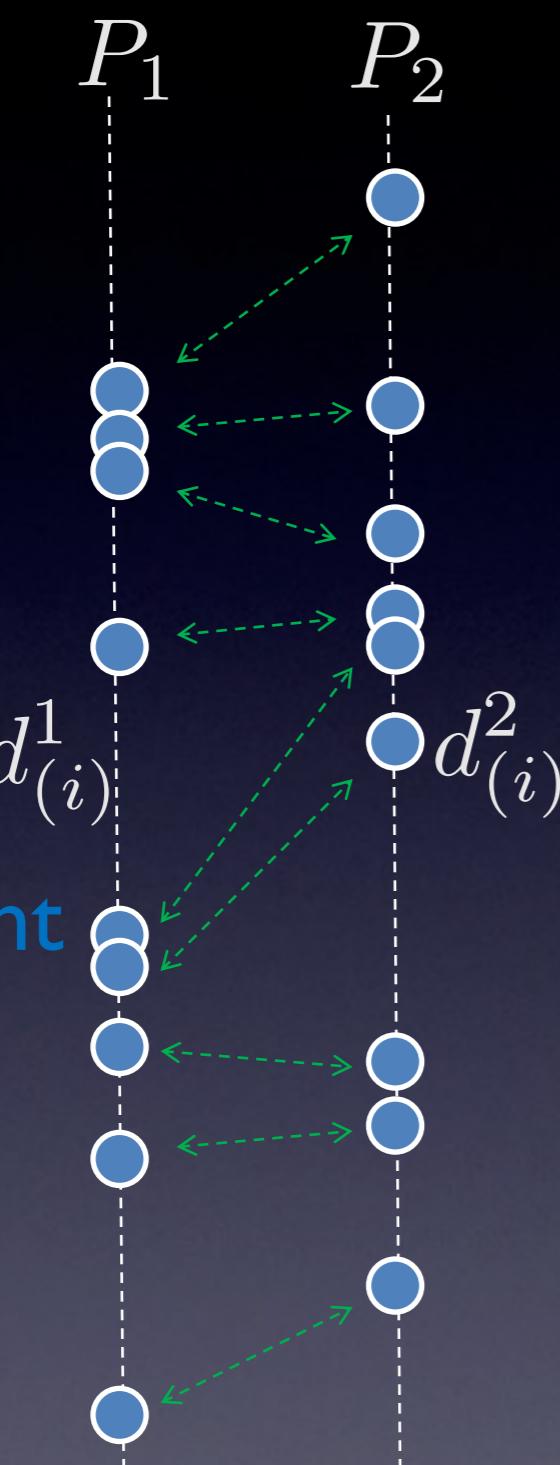


Graph filtration
 $\mathcal{O}(q \log q)$

Wasserstein distance for graph filtrations

WS_pdist2.m

ID
persistent
diagram

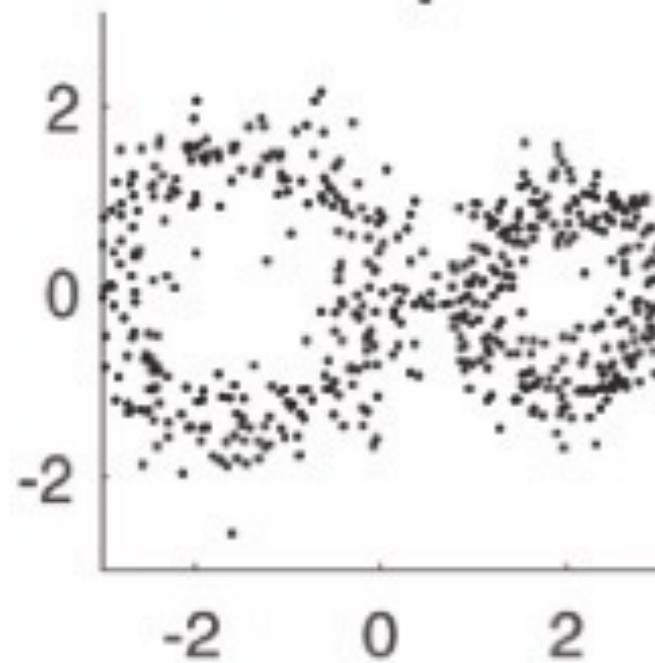


$$\mathcal{D}_0(P_1, P_2)^2 = \sum_i (b_{(i)}^1 - b_{(i)}^2)^2$$

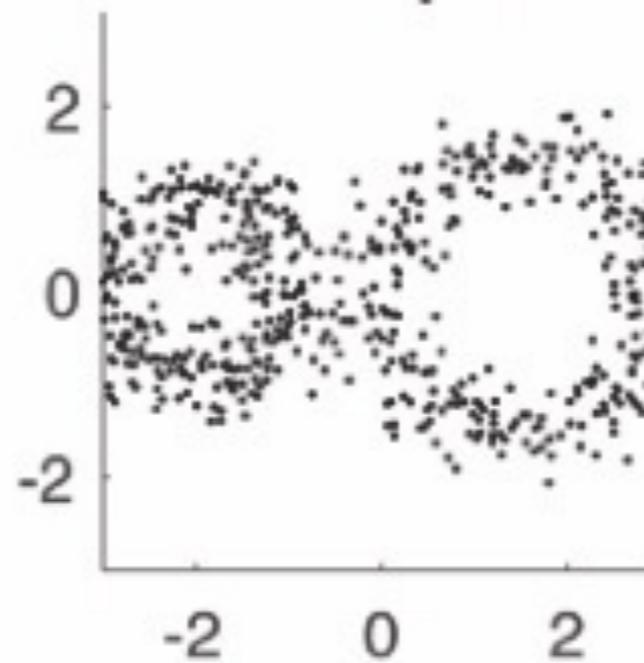
$$\mathcal{D}_1(P_1, P_2)^2 = \sum_i (d_{(i)}^1 - d_{(i)}^2)^2$$

Topologically invariant patterns

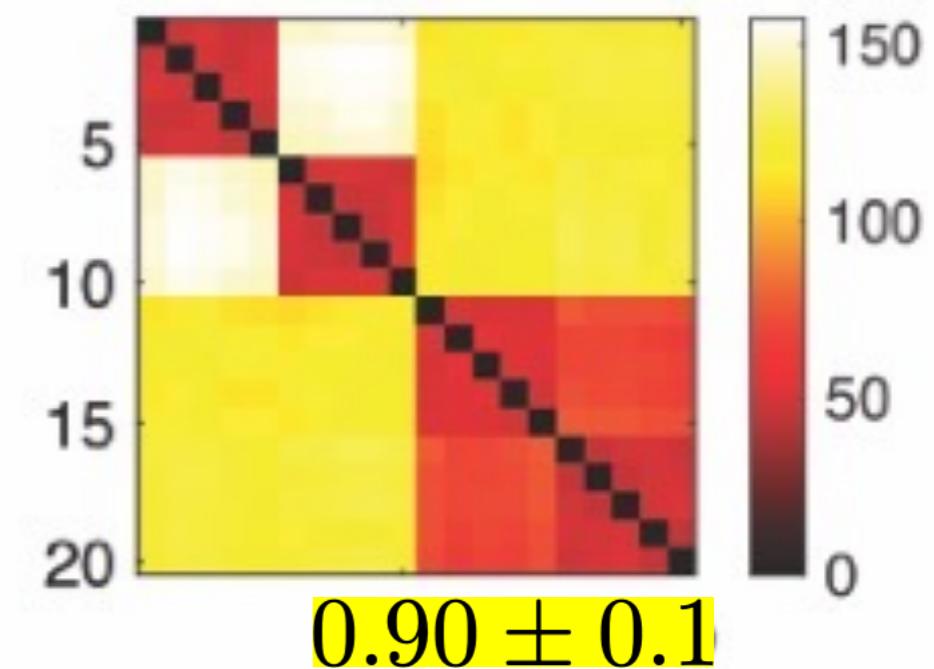
Group 1



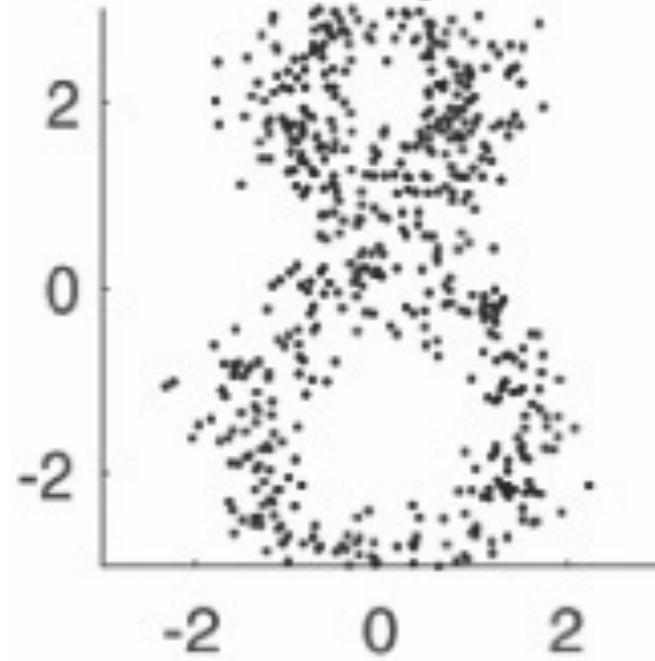
Group 2



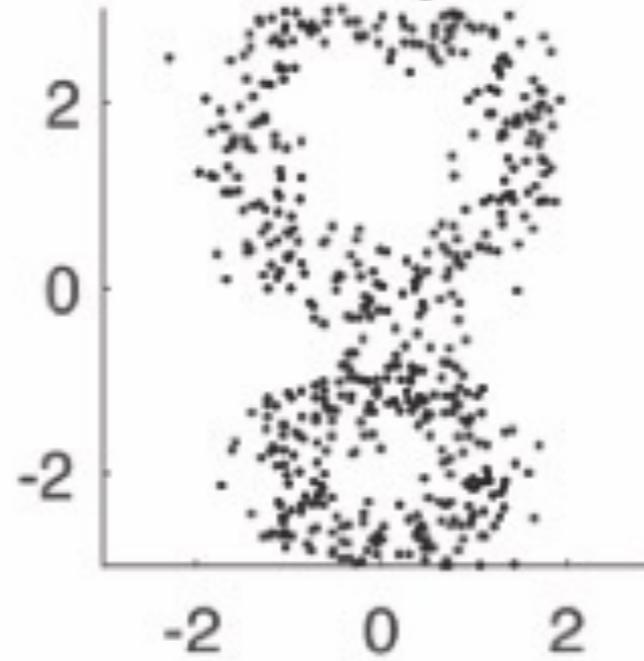
L2-norm



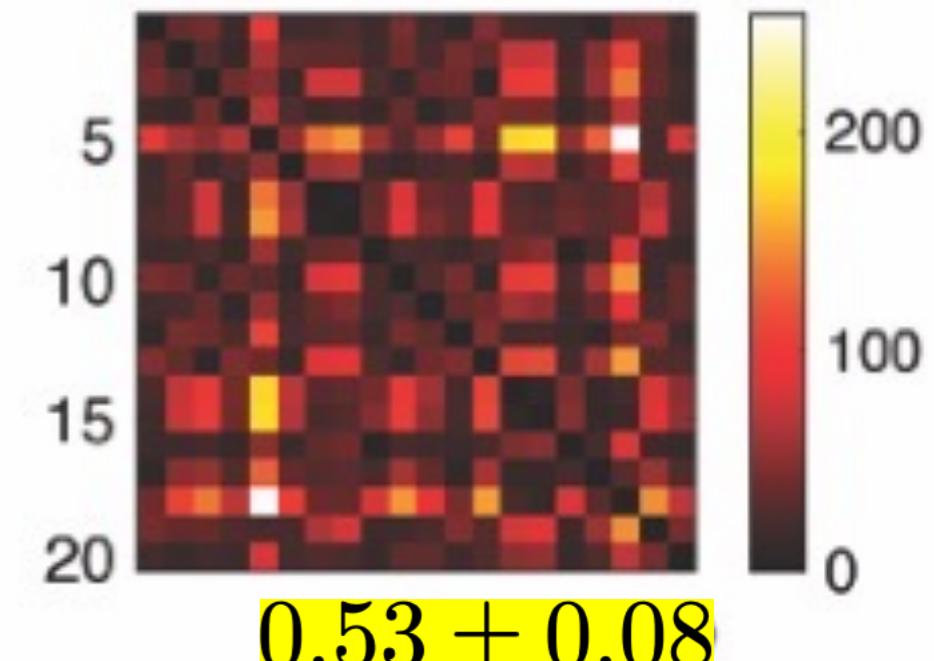
Group 3



Group 4



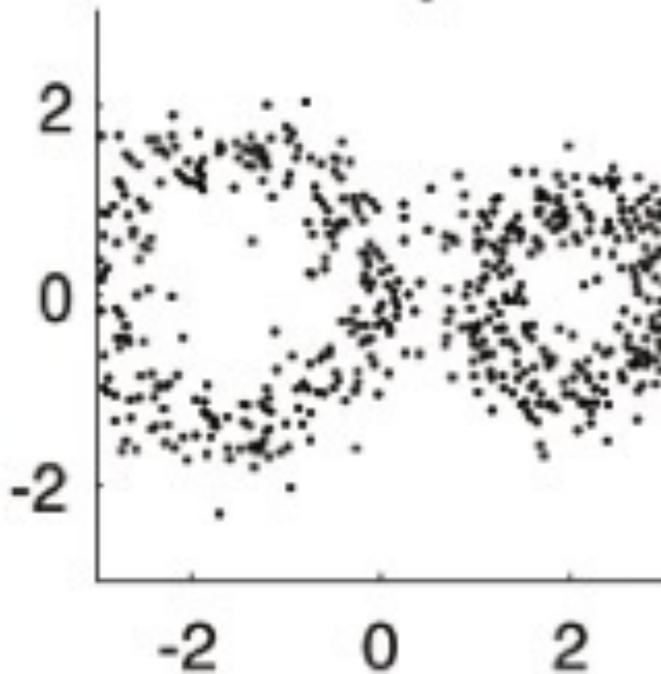
Wasserstein



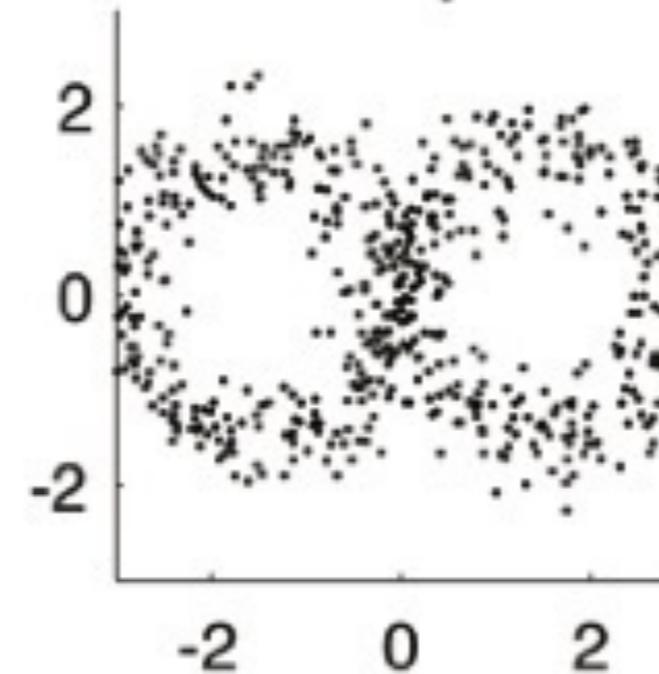
Clustering accuracy

Topologically different patterns

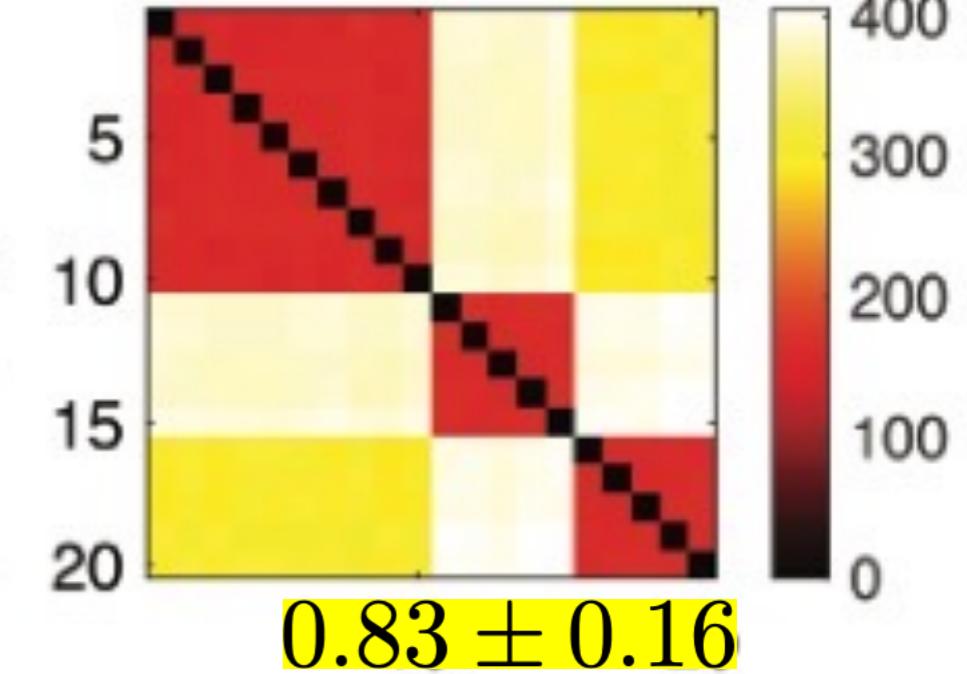
Group 1



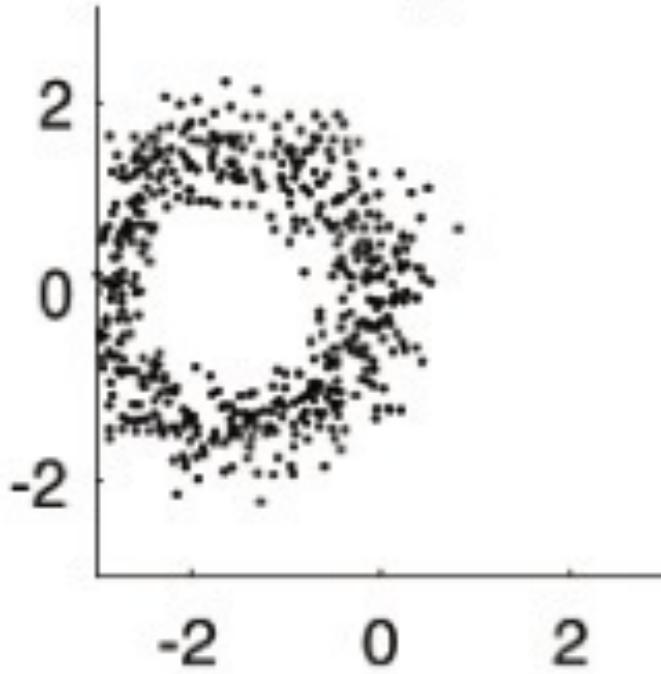
Group 2



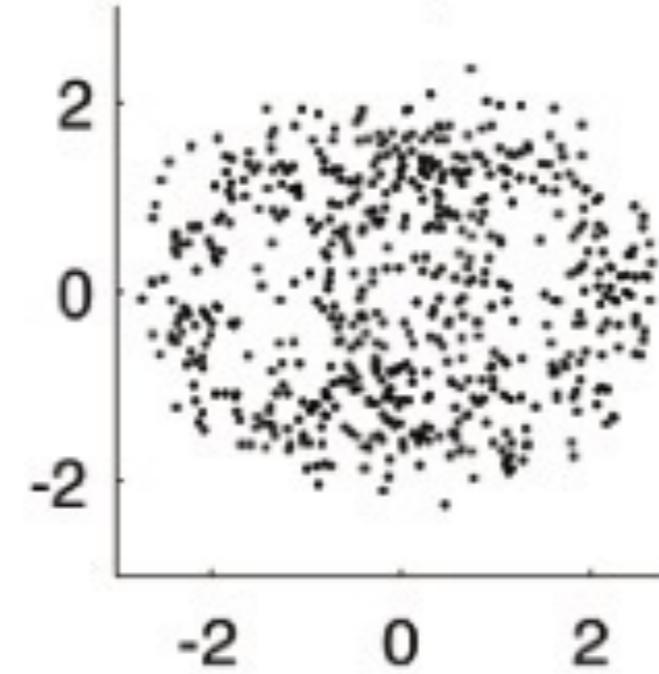
L2-norm



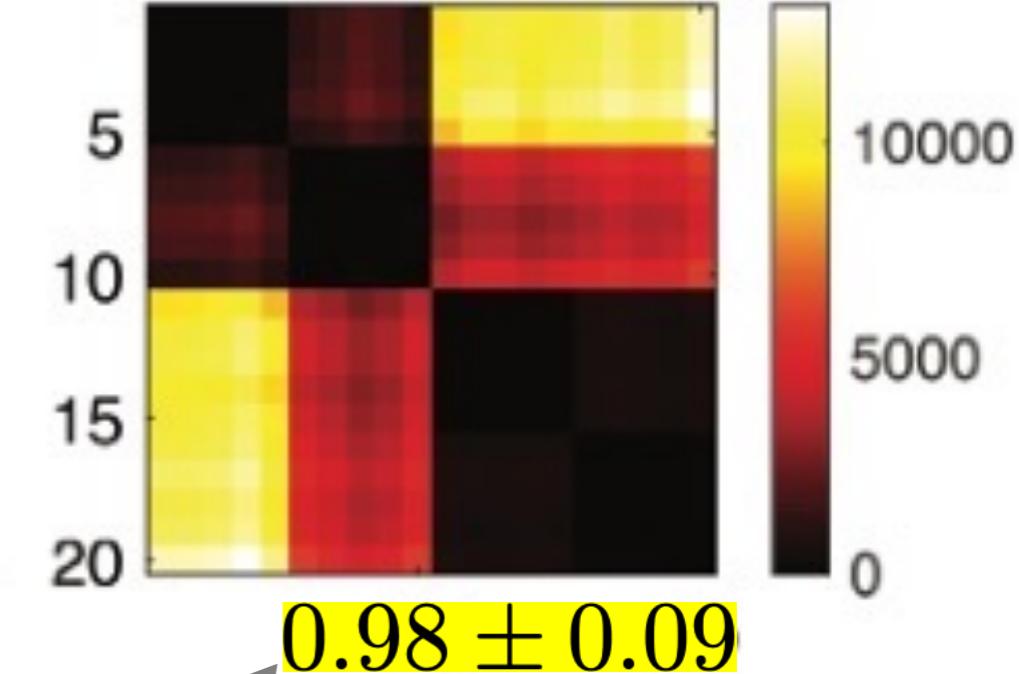
Group 3



Group 4

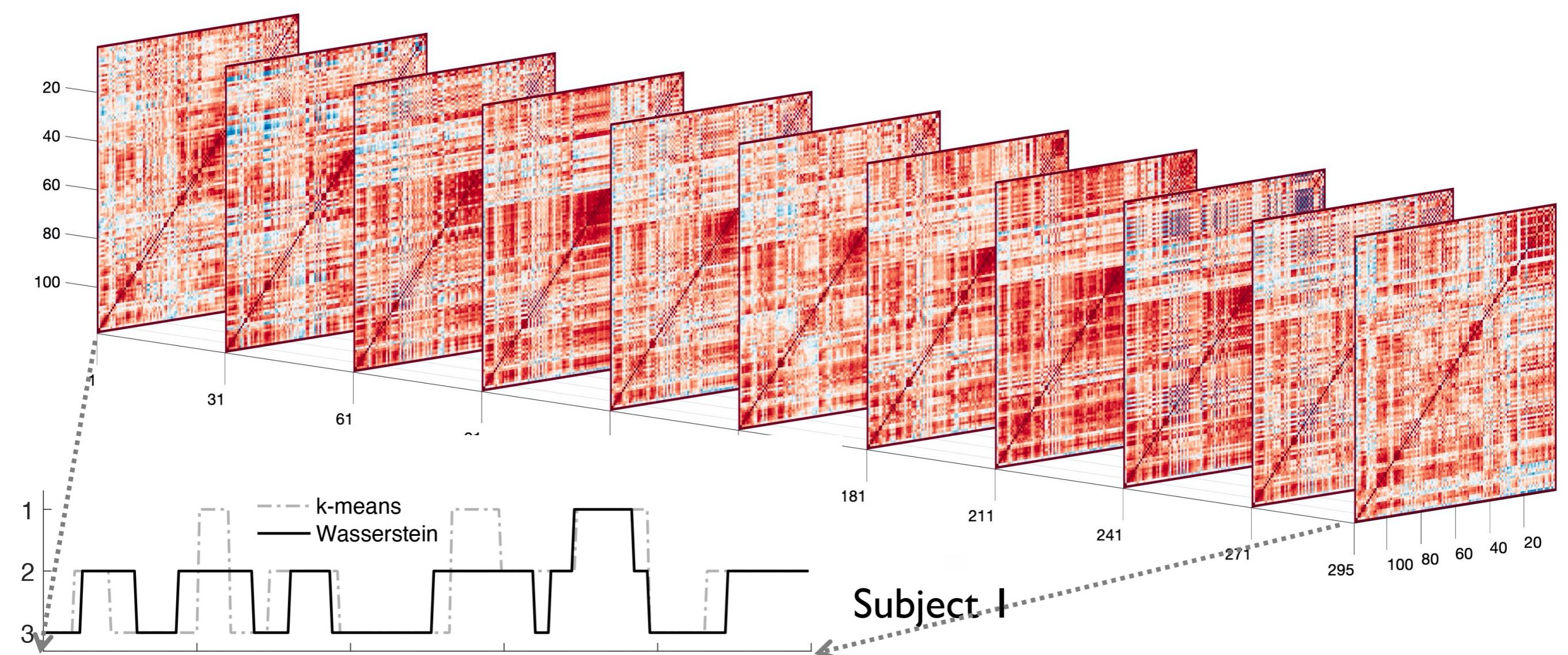


Wasserstein

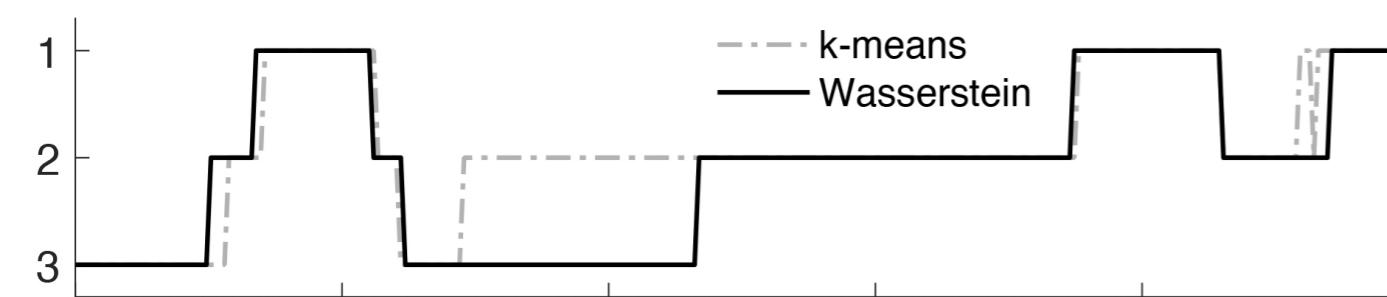


WS_cluster.m

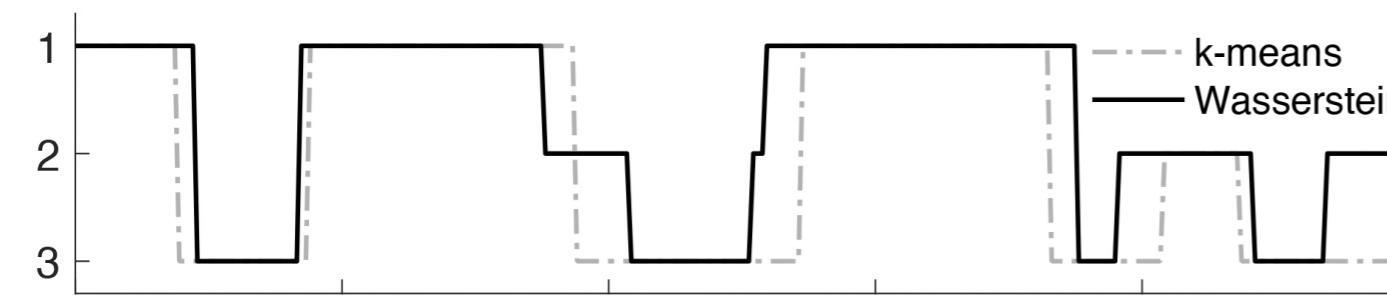
Clustering accuracy



Clustering on
479 subjects

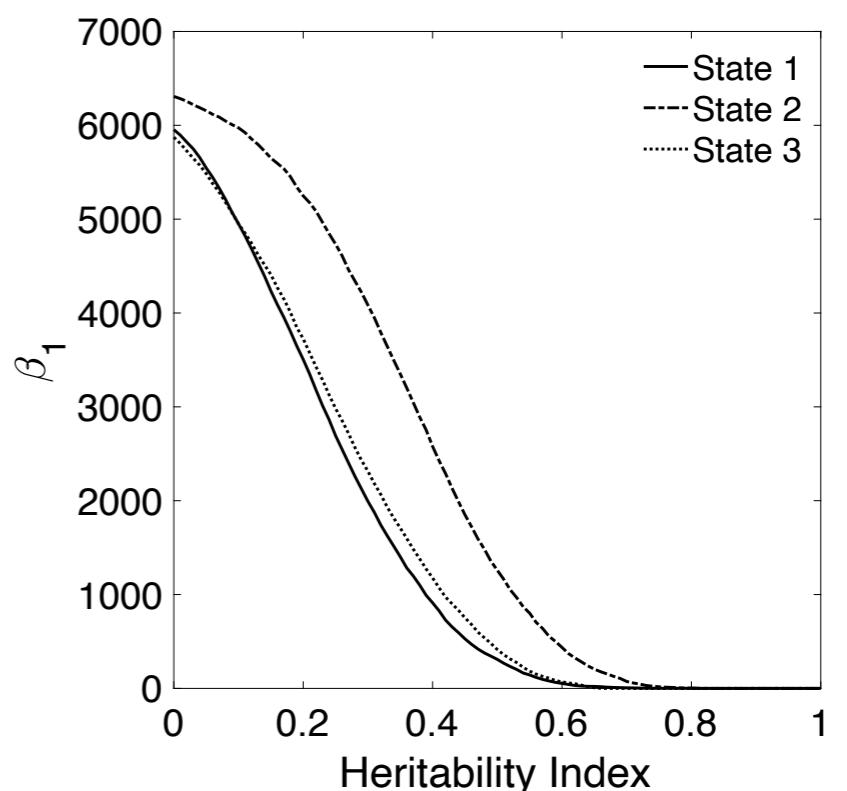
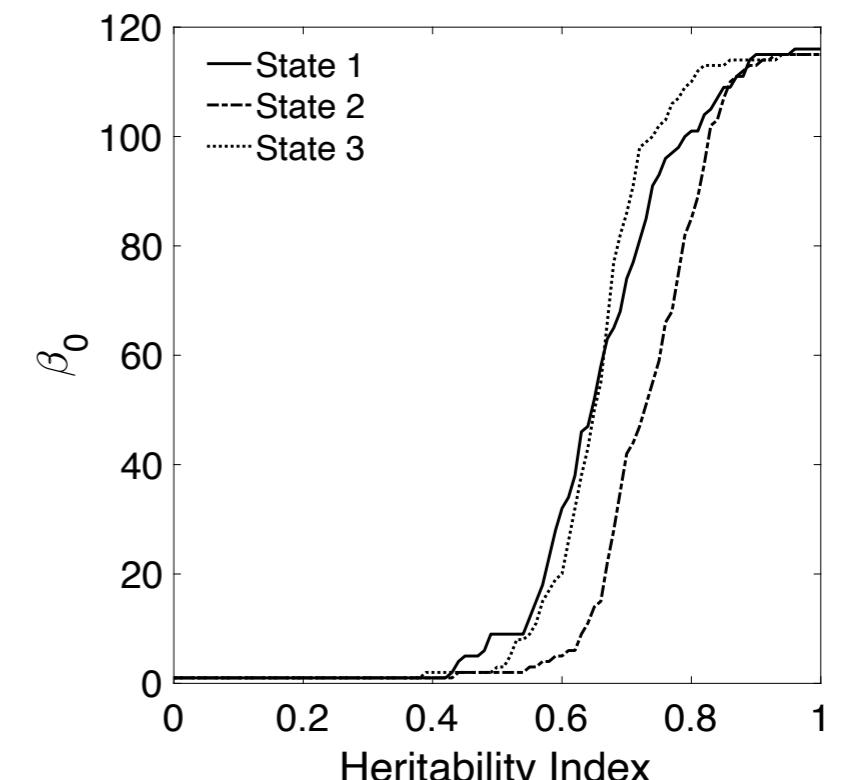
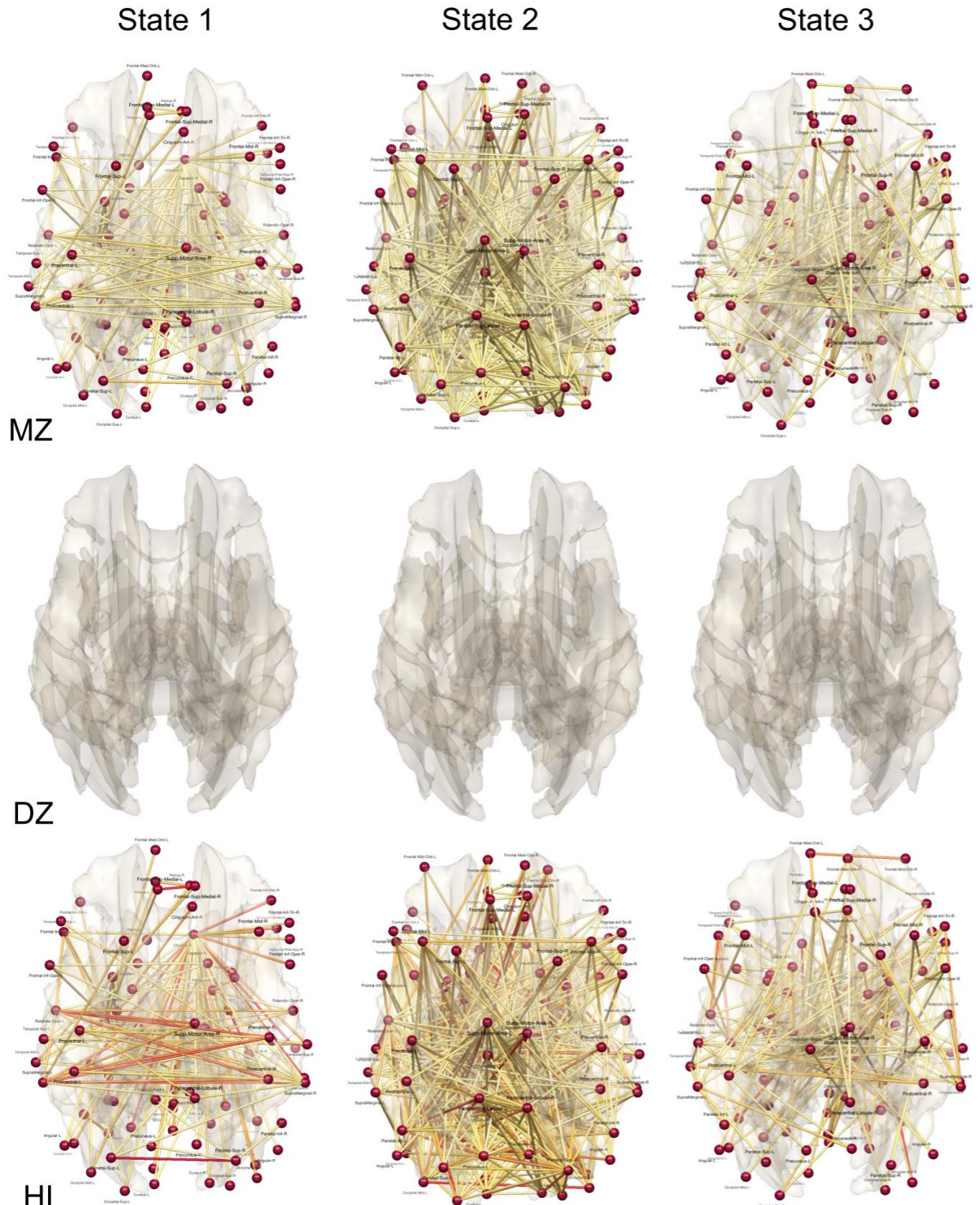


Subject 2

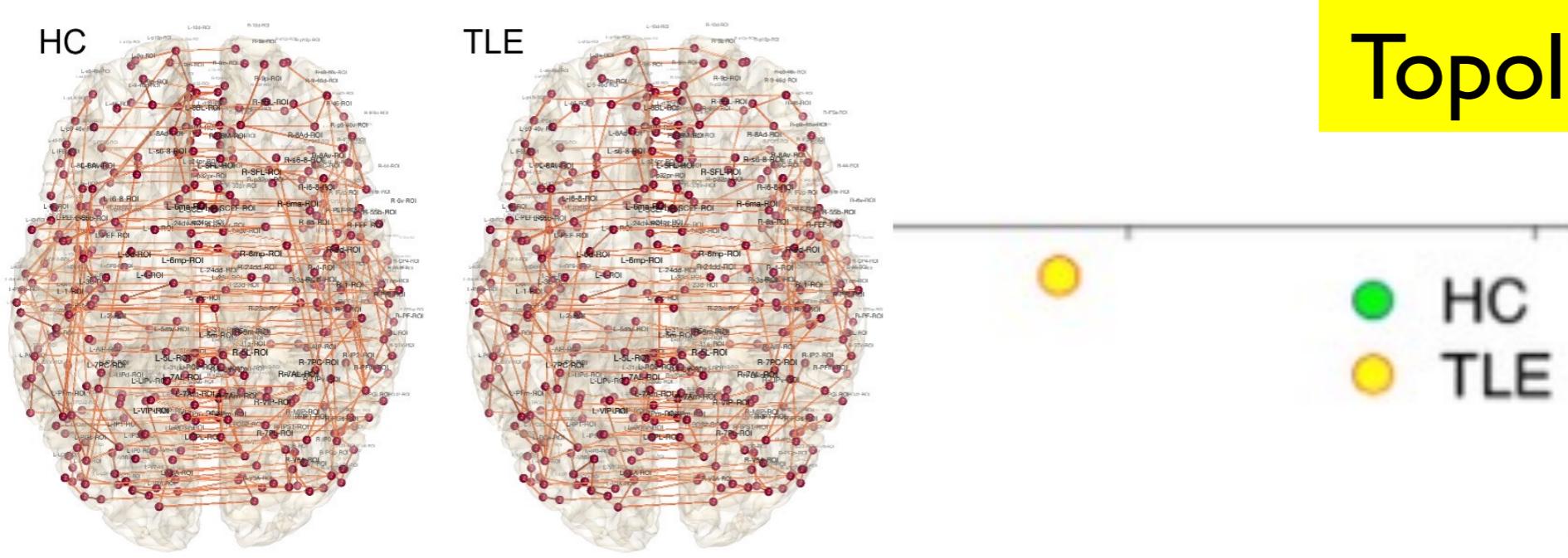


Subject 3

Heritability of state-space of rs-fMRI brain network



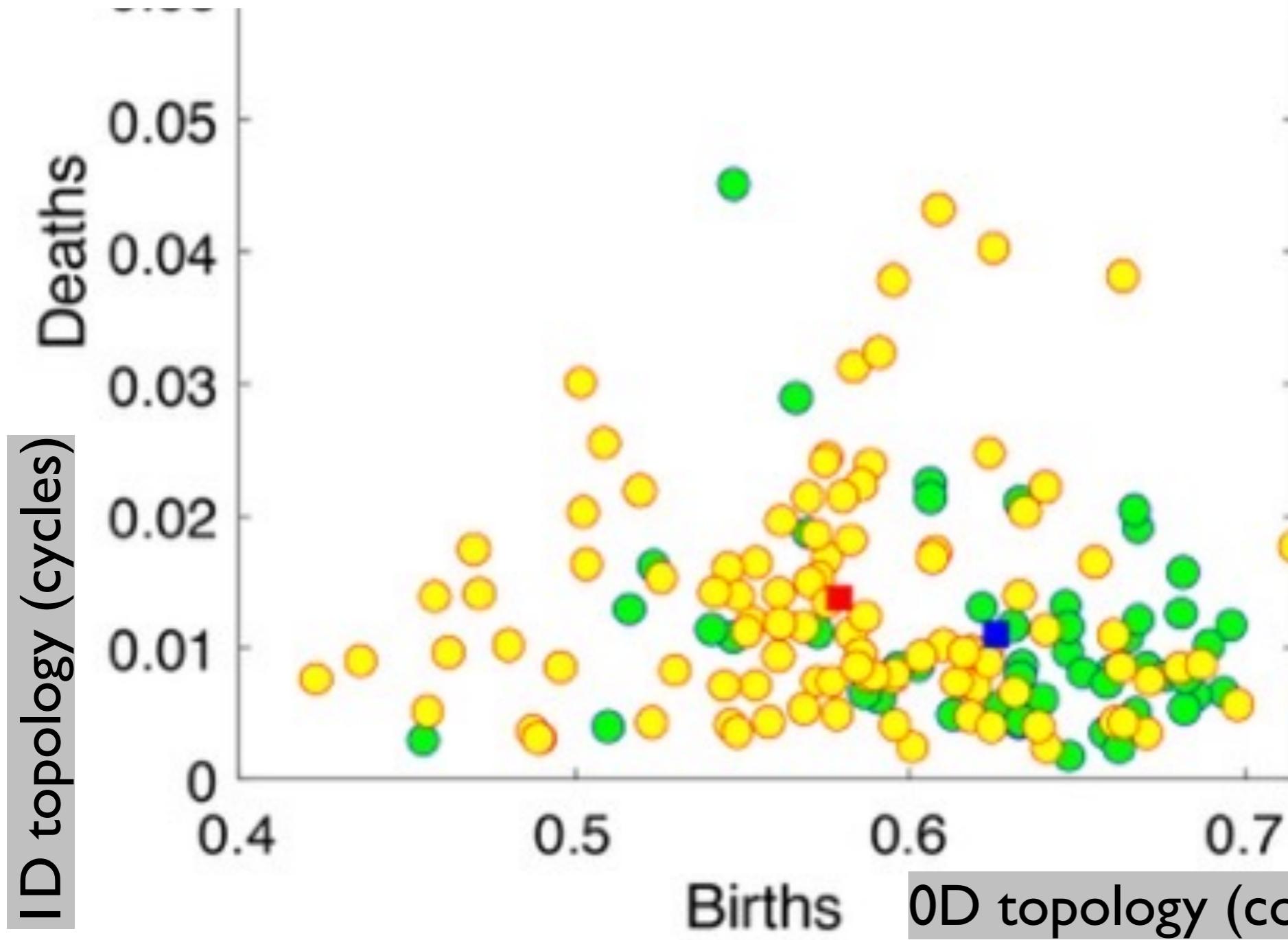
Topological embedding



HC
TLE

Healthy controls
(HC)

Temporal lobe
epilepsy (TLE)



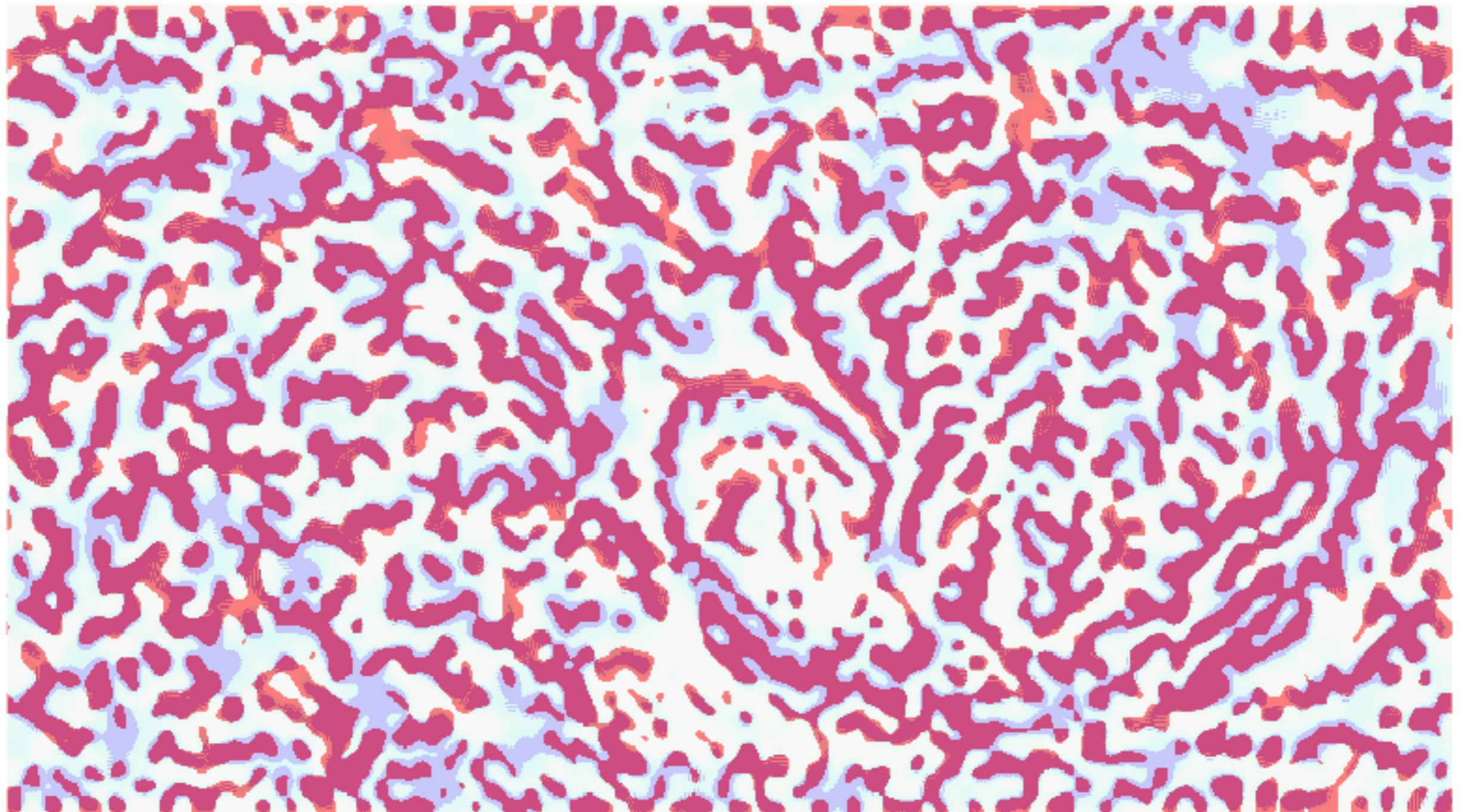
WS_embed.m

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



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)



10th International Congress on Industrial and Applied Mathematics

ICIAM 2023 TOKYO

Thank you.

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

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postdoc and *graduate research*

