# Topological Data Analysis for Brain Networks

## Relating Functional Brain Network Topology to Clinical Measures of Behavior

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# Big Picture

**Goal:** Quantify the relationship between brain functional networks and behavioral measures.

**Our Contribution:** Use topological features based on persistent homology.

**Result:** Combining correlations with topological features gives better prediction of autism severity than using correlations alone.

functional network

behavior

# Motivation

About Autism Spectrum Disorders (ASD):

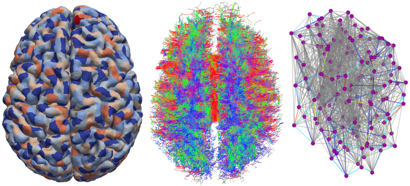
- No cure, causes unknown
- Diagnosis:
  - No systematic method
  - ADOS (Autism Diagnostic Observation Schedule)

Correlate functional brain network to ADOS scores

- Early diagnosis
- Treatment tracking

# What is a Brain Network?

- Represents brain regions and pairwise associations
- Computation of Correlation Matrices:
  - Resting state functional MRI (R-fMRI)
  - Preprocessing
  - Define regions of interest (ROIs)
  - Estimate time series signals
  - Compute pairwise associations - Pearson Correlation



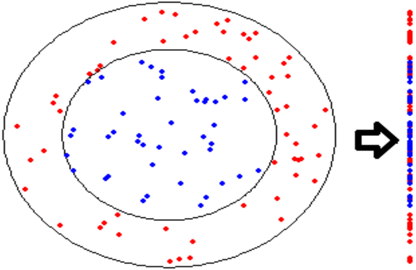
# Why Topology?

How to use this data?

- Graph and graph theoretic measures (e.g. small worldness)
  - Require binary associations (thresholding)
- Correlations as features
  - High dimensionality, not enough samples
- Dimensionality reduction: PCA, random projections
  - May lose structures in higher dimensions

# Why Topology

Projection - may lose structures in higher dimensions



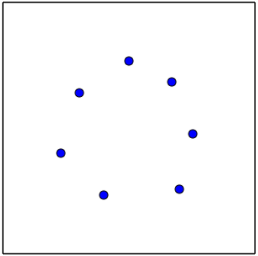
Topology captures structure

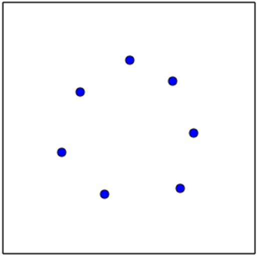
- In higher dimensions
- Across all continuous thresholds

# Persistent Homology

- What are topological features? Homological features:
  - Dim 0 - Connected Components
  - Dim 1 - Tunnels / Loops
  - Dim 2 - Voids
- How to compute them (in a nutshell)?
  - Begin with point cloud
  - Grow balls of diameter $t$ around each point
  - Track features of the union of balls as $t$ increases

# Persistent Homology





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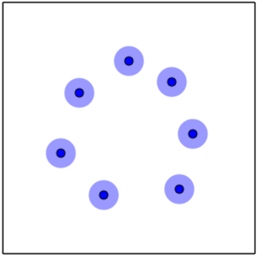

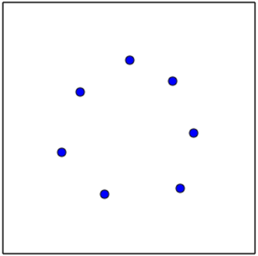

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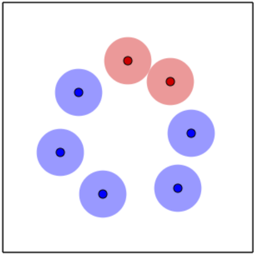

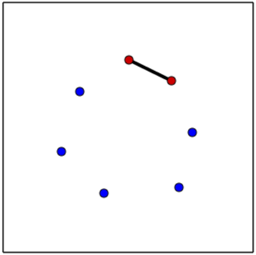

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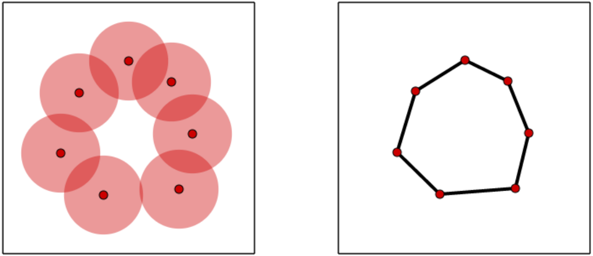

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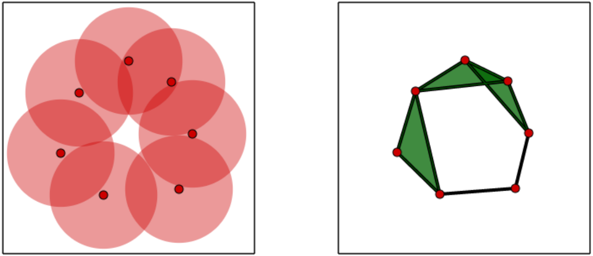

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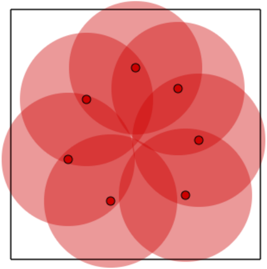
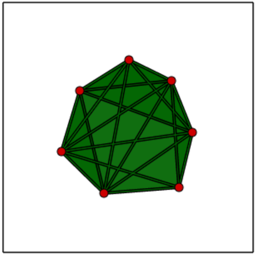




# Persistence Diagrams

Persistent homological features - encoded as barcodes or persistent diagrams

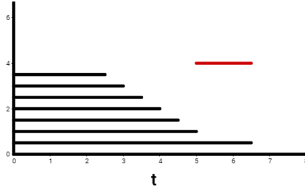



Figure: Barcode

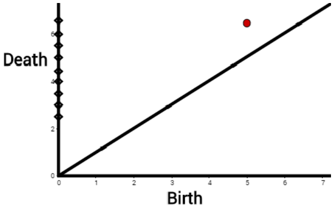
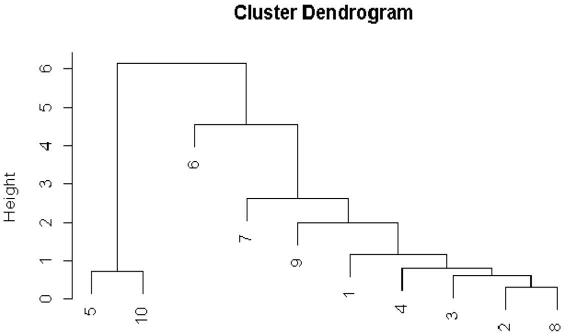
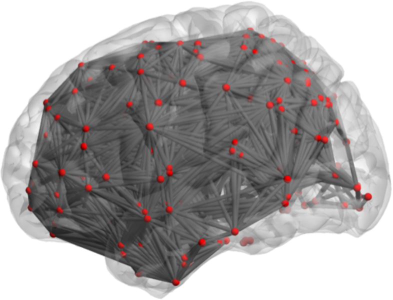


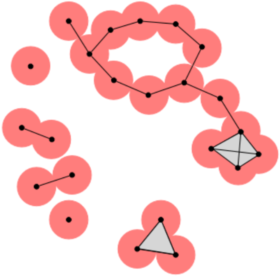

Figure: Persistence Diagram

- Dim 0 features - hierarchical clustering



# Computing Topological Features for Brain Networks





# Partial Least Squares (PLS) Regression

A dimensionality reduction technique that finds two sets of latent dimensions from datasets $X$ and $Y$ such that their **projections** on the latent dimensions are **maximally co-varying**.

- $X$ - features from brain imaging: correlations, topological features (zero mean)
- $Y$ - clinical measure of behavior: ADOS scores (zero mean)

PLS models the relations between $X$ and $Y$ by means of **score vectors**.

# PLS Regression

- $n$ - number of data points
- $X$ - predictor/regressor $(n \times N)$, $Y$ - response $(n \times M)$
- PLS - decompose $X$, $Y$ such that:

$$X = TP^T + E$$
$$Y = UQ^T + F$$

Where

  - $T, U$ - latent variables/score vectors $(n \times p)$, factor matrices
  - $P$ $(N \times p)$, $Q$ $(M \times p)$ - orthogonal loading matrices
  - $E$ $(n \times N)$, $F$ $(n \times M)$ - residuals/errors

- $T, U$ are chosen such that projections of $X, Y$, that is, $T$ and $U$, are maximally co-varying.

# PLS Regression: the Algorithm

Iterative NIPALS[1] algorithm

- Find first latent dimension

  i.e. find vectors $w, c$ such that

$$t = Xw, \quad u = Yc$$

  have maximal covariance

- Deflate previous latent dimensions from $X$, $Y$ and repeat

[1] **Nonlinear iterative partial least squares**; **[Wold 1975]**.

# Kernel PLS

Kernel form of NIPALS algorithm (kPLS)

1. Initialize random vector $u$
2. Repeat until convergence
   (a) $t = Ku/\|Ku\|$
   (b) $c = Y^T t$
   (c) $u = Yc/\|Yc\|$
3. Deflate $K = (I - tt^T)K(I - tt^t)$
4. Repeat to compute subsequent latent dimensions

# Data

- 87 Subjects: 30 Control, 57 ASD
- ADOS scores: 0 to 21
- 264 ROIs (Power regions)
- $264 \times 264$ correlation matrix.
- 34,716 distinct pairwise correlations per subject.

# Experiments

- Given: Correlation matrices
- Map to metric space

$$d(x,y) = \sqrt{1 - \mathrm{Cor}(x,y)}$$

- Compute persistence diagrams
- Define inner product of persistence diagrams[2] (i.e. kernel):
  Given two persistence diagrams $F$, $G$

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

where for every $q = (x,y) \in G$, $\bar{q} = (y,x)$

[2] **[Reininghaus Huber Bauer Kwitt 2015]**.

# Experiments

Performed experiments with 3 kernels:

1. $K^{Cor}$ - Euclidean dot product of vectorized correlations
2. $K^{TDA} = w_0 K^{TDA_0} + (1 - w_0) K^{TDA_1}$
    - $K^{TDA_0}$ - using only Dim 0 features
    - $K^{TDA_1}$ - using only Dim 1 features
3. $K^{TDA+Cor} = w_0 K^{TDA_0} + w_1 K^{TDA_1} + (1 - w_0 - w_1) K^{Cor}$

Baseline predictor - mean ADOS score

- Leave one out cross validation over parameters
  - $\sigma_0$, $\sigma_1$ - ($\log_{10}\sigma$) from -8.0 to 6.0 by 0.2
  - $w_0, w_1$ - from 0.0 to 1.0 by 0.05
- $k^{TDA}$ parameters: $\sigma_0 = -6.6$, $\sigma_1 = 1.8$, $w_1 = 0.95$
- $k^{TDA+Cor}$ parameters: $\sigma_0 = -7.8$, $\sigma_1 = 2.8$, $w_0 = 0.1$, $w_1 = 0.4$
- Compute RMSE
- Permutation test for significance

# Results

Result Highlights:

- Baseline RMSE: 6.4302
- $K^{TDA+Cor}$:
  - Only method statistically significant over baseline
  - Permutation test p-value: 0.048
  - RMSE: 6.0156

# Conclusion

- Augmenting correlations with topological features gives a **better** prediction of autism severity than using correlations alone
- Topological features derived from R-fMRI have the **potential** to explain the connection between functional brain networks and autism severity

# Future Work

Many things to try

- Alternatives to correlation
- Different distance metric
- Different kernel
- Multi-site data

# Publication

*Kernel Partial Least Squares Regression for Relating Functional Brian Network Topology to Clinical Measures of Behavior*

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# Thank you!

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