Harmonic Holes as the Submodules of Brain Network and Network Dissimilarity

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Seoul National University Hospital, Republic of Korea
Hyekyoung Lee
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• Moo K. Chung (University of Wisconsin-Madison, USA)
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• Yu Kyeong Kim (SMG-SNU Boramae Medical Center)
• Dong Soo Lee (Seoul National University Hospital)
Outline

I. Brain imaging data analysis
   • FDG-PET
   • Brain connectivity
   • ADNI dataset

II. Network distance based on persistent homology
   • Persistent homology
   • Bottleneck distance
   • Gromov-Hausdorff (GH) distance on single linkage matrix
   • Kolmogorov-Smirnov (KS) distance of connected components and cycles
   • Harmonic hole (HH) dissimilarity

III. Results and conclusions
I. Brain imaging data
Brain imaging data in macroscale

- **Functional data**
  - EEG/MEG
  - PET
  - fMRI
  - Electrical activity
  - Metabolic response
  - Hemodynamic response

- **Structural data**
  - MRI
  - Gray/white matter density or volume
  - White matter tracts

- DTI
FDG-PET

- Radioactive material, called FDG is injected into a subject.
- FDG becomes trapped in neurons.
- PET measures the FDG uptake.
- FDG uptake ↑, neuronal activity ↑
Three dimensional data

Dimension: 91 x 109 x 91

Number of voxels >> 200,000

(From http://pds21.egloos.com/pds/201108/19/90/c0134890_4e4dfab480d6b.jpg)
Brain connectivity

Human Connectome

a map of the neural connections within the brain
(Olaf Sporns, 2005)

Functional connectivity based on PET

If two regions are simultaneously changed (correlated) across subjects, they may be connected.
Node set

Predefined anatomical atlas

Region of interest (ROI),
90~130 ROIs

- Location of a node: center of ROI
- Measurement of a node: average of voxel intensities in a ROI
Edge weight

Distance matrix

Distance = sqrt(1 – corr(f_i, f_j))
Data set we used

• Alzheimer's Disease Neuroimaging Initiative (ADNI) data
• Public data: http://adni.loni.usc.edu
• FDG-PET data
• Normal controls (NC): 181 subjects
• Mild cognitive impairment (MCI)
  • Stable MCI who were remained stable after 3 years (sMCI): 91 subjects
  • Progressive MCI who were progressed to AD after 3 years (pMCI): 77 subjects
• Alzheimer’s disease (AD): 135 subjects
What we want to do

- Clustering based on network distance

NC  sMCI  pMCI  AD

- Which parts of brain connectivity make the difference
II. Network distance based on persistent homology
Threshold

(Lee, TMI2012, MICCAI2011)

Different adjacency matrices are constructed depending on the thresholds.

Which network will you use?

Distance Matrix

threshold

Adjacency Matrix
Persistent homology
Persistence diagram

Connected components

Holes
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III. Results and conclusions
Kolmogorov-Smirnov (KS) distance

(Chung, IPMI2017, ISBI2018)

Maximum difference between two curves

# Connected Components

0 1 2 3 4 5 6

0 1.0 1.25 1.5 1.75 2.0

KS0

β0-curve

cycle-curve

# Cycles

0 1 2 3 4 5 6 7 8 9 10

0 1.8 2.0 2.25 2.5 2.75 3.0

KS1
Bottleneck distance

Given two persistence diagrams $X$ and $Y$, their bottleneck distance is defined as

$$W_\infty(X, Y) = \inf_{\eta:X \to Y} \sup_{x \in X} \|x - \eta(x)\|_\infty,$$

where $\eta$ ranges over all bijections and $\|(x, y)\|_\infty = \max\{|x|, |y|\}$ is the usual $L_\infty$-norm. Similarly, the $q$-th Wasserstein distance is defined as

$$W_q(X, Y) = \left[ \inf_{\eta:X \to Y} \sum_{x \in X} \|x - \eta(x)\|_\infty^q \right]^{1/q}.$$

Ref: Geometry Helps to Compare Persistence Diagrams*
Michael Kerber† Dmitriy Morozov‡ Arnur Nigmetov§
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III. Results and conclusions
Single Linkage Matrix

(Carlsson, 2010)

Graph filtration

$\epsilon_1 = 1$

$\epsilon_2 = 1.2$

$\epsilon_3 = 1.3$

$\epsilon_4 = 1.4$
Gromov-Hausdorff Distance

(Lee, TMI2012, MICCAI2011)

Maximum difference between two single linkage matrices
Harmonic hole (HH) dissimilarity

- Each point in a persistence diagram represents a hole.
- A harmonic hole is an eigenvector with zero eigenvalue of combinatorial Hodge Laplacian.
- So, if a harmonic hole is denoted by $x$, $x'x = 1$.
- If two different harmonic holes are denoted by $x$ and $y$, their dissimilarity is estimated by $1 - |x'y|$.
- In bottleneck distance, the distance between two holes is estimated by the distance between two points in persistence diagram.
- In HH dissimilarity, the distance between two holes is estimated by $1 - |x'y|$.
• We first estimate the correspondence of harmonic holes between two networks by minimizing the sum of dissimilarities, $1 - |x'y|$. 
• The average of distances between two corresponding harmonic holes becomes HH dissimilarity.
III. Results
Network distances and clustering accuracy
Citation of HHs within a group
Citation of HHs within a group
Citations of HHs between groups

(a) (top) Clustering of the 600 most cited holes between sMCI and pMCI

(b) (Left) Harmonic hole in sMCI and the corresponding holes in pMCI in cluster 1, 2, 3, and 4
Conclusions

• In this study, we propose a new method of measuring network differences based on the dissimilarity measure of harmonic holes (HHs).

• We also find the most contributed HHs to the network difference based on the HH dissimilarity.

• We applied our proposed method to clustering the networks of 4 groups in ADNI data, normal controls (NC), stable and progressive mild cognitive impairment (sMCI and pMCI), and Alzheimer’s disease (AD).

• The results showed that the clustering performance of the proposed method was better than that of network distances based on only the global change of topology.
Thank you for your attention!!

leehk.brain@gmail.com