Mapping Brain Structural Connectivities to Functional Networks via Graph Encoder-Decoder

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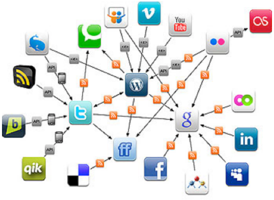
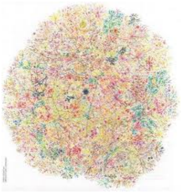
Network Science analytics

Online social media



Internet



Clean energy and grid analytics

- Network as graph $G = (\mathcal{V}, \mathcal{E})$: encode pairwise relationships
- Desiderata: Process, analyze and learn from network data [Kolaczyk'09]
  - $\Rightarrow$ Use G to study graph signals, data associated with nodes in $\mathcal{V}$
- Ex: Opinion profile, buffer congestion levels, **brain signal analyses**

Networks of the brain

- Challenge: understand human brain function and structure
  - Neuroimaging advances $\Rightarrow$ Data increase in volume and complexity
  - Graph-centric analysis and methods of network science [Sporns'10]

- Brain networks can reflect two connectivity patterns
  - Structural connectivity (SC). How is the brain wired?
    $\Rightarrow$ Anatomical tracts connecting brain regions (DTI)
  - Functional connectivity (FC). How the brain functions?
    $\Rightarrow$ Correlation between neural signals in different regions (fMRI)

- Key problem: deciphering the relationship between SC and FC
  - Simulations of nonlinear cortical activity models [Honey et al'09]
  - Diffusion-based parametric inverse problem [Abdelnour et al'14]
  - Network deconvolution [Li-Mateos'19]

- **Goal:** pursue SC-to-FC mapping as a regression problem

  $\Rightarrow$ Reconstruct FC network from SC network

Graph signal processing (GSP)

- Graph $G(\mathcal{V},\mathcal{E})$ with $N = |\mathcal{V}|$ nodes $\Rightarrow$ $\mathbf{A}$ and $\mathbf{L} = \mathbf{D} - \mathbf{A}$
- Graph signals mappings $x : \mathcal{V} \rightarrow \mathbb{R}$, represented as vectors $\mathbf{x} \in \mathbb{R}^N$
- To understand GS $\Rightarrow$ Graph-shift operator $\mathbf{S} \in \mathbb{R}^{N\times N}$
  - $\Rightarrow$ Local $S_{ij} = 0$ for $i \neq j$ and $(i,j) \notin \mathcal{E}$ $\Rightarrow$ Ex: $\mathbf{A}$ or $\mathbf{L}$
  - $\Rightarrow$ Spectrum of $\mathbf{S} = \mathbf{U}\mathbf{\Lambda}\mathbf{U}^T$
- Graph Fourier Transform (GFT): $\tilde{\mathbf{x}} = \mathbf{U}^T\mathbf{x}$
- Generalize machine learning models for network data
  - $\Rightarrow$ GSP to define convolutions on graphs [Ortega et al'19]
  - $\Rightarrow$ Tool to integrate brain structure and function [Wang et al'19]

Graph convolutions

- Given a graph filter $\mathbf{h}$, graph convolution operator

$$\mathbf{x} * \mathbf{h} = \mathbf{U}((\mathbf{U}^T\mathbf{h}) \odot (\mathbf{U}^T\mathbf{x})) = \mathbf{U}g_\theta(\boldsymbol{\Lambda})\mathbf{U}^T\mathbf{x}$$

- ChebNet: Chebyshev polynomials of $\boldsymbol{\Lambda}$ [Defferrard et al'16]

$$g_\theta(\tilde{\boldsymbol{\Lambda}}) = \sum_{i=0}^{K} \theta_i T_i(\tilde{\boldsymbol{\Lambda}})$$

  - θ_i: polynomial filter coefficients to be learned
  - $\tilde{\boldsymbol{\Lambda}} = 2\boldsymbol{\Lambda}/\lambda_{\max} - \mathbf{I}_N$, $\lambda_{\max}$: largest eigenvalue of $\mathbf{L}$
  - $T_k(x) = 2xT_{k-1}(x) - T_{k-2}(x)$ with $T_0(x) = 1$, $T_1(x) = x$

- Graph convolution operator becomes $(\tilde{\mathbf{L}} = (2/\lambda_{\max})\mathbf{L} - \mathbf{I}_N)$

$$\mathbf{x} * \mathbf{h} = \sum_{i=0}^{K} \theta_i T_i(\tilde{\mathbf{L}})\mathbf{x}$$

  - Combines signal values at nodes K-hops away in G

Graph convolutional network (GCN)

- First-order approximation of ChebNet [Kipf-Welling'17]
  - Set $K = 1$, $\lambda_{\text{max}} = 2$, $\theta = \theta_0 = -\theta_1$

$$\mathbf{x} * \mathbf{h} = \theta(\mathbf{I}_N + \mathbf{D}^{-1/2}\mathbf{A}\mathbf{D}^{-1/2})\mathbf{x}$$

- Compact rule for per-layer filtering update

$$\tilde{\mathbf{X}} \leftarrow \tilde{\mathbf{A}}\mathbf{X}\boldsymbol{\Theta}$$

  - $\tilde{\mathbf{A}} = \mathbf{I}_N + \mathbf{D}^{-1/2}\mathbf{A}\mathbf{D}^{-1/2}$
  - $\mathbf{X}$: set of multiple observations of the graph signal $\mathbf{x}$
  - $\boldsymbol{\Theta}$ collects the learnable filter parameters

- $\tilde{\mathbf{X}}$ integrates nodal attributes in $\mathbf{X}$ and topology in $\tilde{\mathbf{A}}$

- Q: Aggregate information from multiple hops within G?

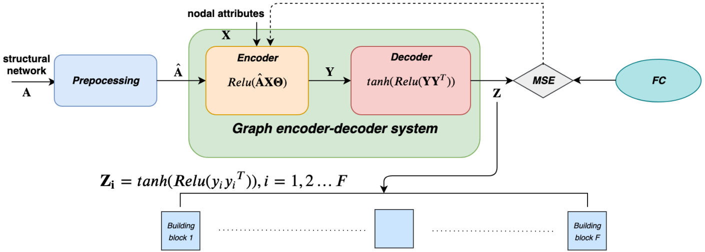
  $\Rightarrow$ Stack convolutional layers with pointwise non-linear activation

  $\Rightarrow$ Capture *indirect interactions* across the network

Problem statement

Study the generation of FC patterns from SC graphs

- Goal: learn the mapping from brain SC networks to FC networks
- Approach: reconstruct FC networks from the given SC networks
- Model: GCN-based encoder-decoder system



- Analysis: investigate latent variables within the system

Model architecture: Encoder

- Input SC network $\mathbf{A} \in \mathbb{R}^{N \times N}$, N regions from brain atlas
  - $\Rightarrow$ Edge weights represent SC between brain regions
  - $\Rightarrow$ Preprocessing: $\hat{\mathbf{A}} := \tilde{\mathbf{D}}^{-1/2} \tilde{\mathbf{A}} \tilde{\mathbf{D}}^{-1/2}$, $\tilde{\mathbf{A}} = \mathbf{I} + \mathbf{A}$

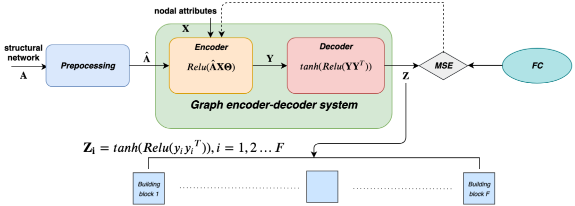
- Learn vertex representations (i.e., embeddings) that capture
  (i) Nodal attributes, e.g. intrinsic properties of brain regions
  (ii) Graph topology information, e.g. regional connection strengths

- A single-layer GCN used for encoder to learn node embeddings

$$\mathbf{Y} = \mathrm{Relu}(\hat{\mathbf{A}} \mathbf{X} \boldsymbol{\Theta}) \in \mathbb{R}^{N \times F}$$

  - $\mathbf{X} \in \mathbb{R}^{N \times T}$: input signal matrix
  - $\boldsymbol{\Theta} \in \mathbb{R}^{T \times F}$: learnable GCN filter coefficients
  - $\mathrm{Relu}(x) = \max(0, x)$ activation for training the network

Model architecture: Decoder

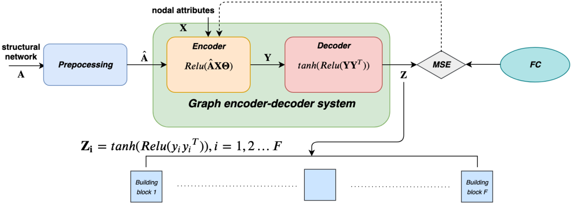


- Node embeddings $\mathbf{Y} \in \mathbb{R}^{N \times F}$ go through the outer-product decoder

$$\mathbf{Z} = \tanh(\mathrm{Relu}(\mathbf{Y}\mathbf{Y}^T)) \in \mathbb{R}^{N \times N}$$

- Weights in empirical FC networks restricted to [0,1]
  - Ensure the output of the decoder in the same range
  - Choose tanh and Relu over Sigmoid
- Loss function: MSE between $\mathbf{Z}$ and empirical FC

Model architecture: Latent variables



- $\mathbf{YY}^T$: rank-F approximation of FC graph before activation
  - Extract and analyze each of the rank-1 components $\mathbf{y}_i\mathbf{y}_i^T$

$$\mathbf{Z}_i = \tanh(\mathrm{Relu}(\mathbf{y}_i\mathbf{y}_i^T)), \quad i = 1, \ldots, F$$

- $\mathbf{Z}_i \Leftrightarrow$ outputs of individual filters in graph convolutional layer

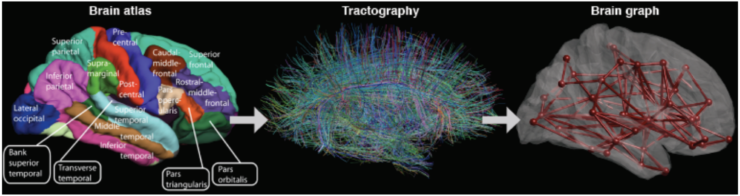
  $\Rightarrow$ View as building blocks of FC network

- Reveal details about generation of FC patterns from SC networks

Numerical tests: Data

- 1058 healthy subjects from Human Connectome Project (HCP)
- Preprocessed SC network $\mathbf{A}$ from diffusion MRI

  $\Rightarrow$ Fiber counts between $N = 68$ cortical surface regions



- Preprocessed FC network from functional MRI

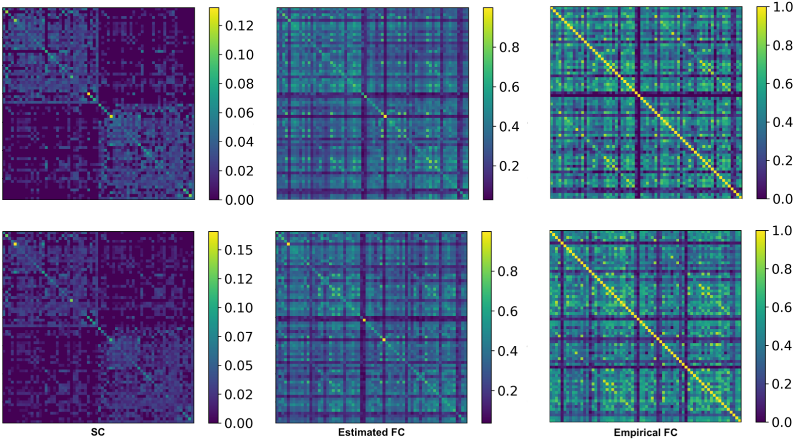
  $\Rightarrow$ Blood oxygen-level dependent (BOLD) signals

  $\Rightarrow$ Estimated FC $\Leftrightarrow$ Pearson correlation between BOLD signals

- One-hot encoding as the signal on each graph node $(\mathbf{X} = \mathbf{I}_N)$

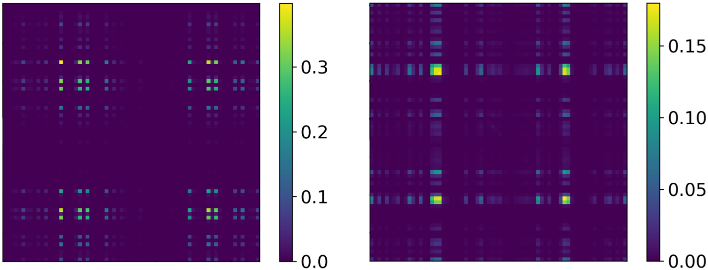
Numerical tests: FC reconstruction performance

- MSE between reconstructed and empirical FC networks
  - Average test reconstruction error $= 0.0304$ with std $= 0.0011$
  - Capture population patterns of SC-FC relationship



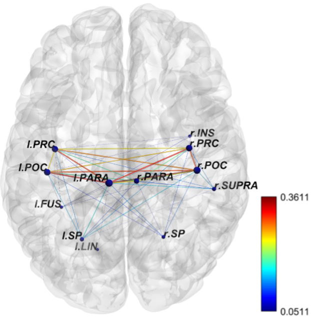
Numerical tests: Component graphs

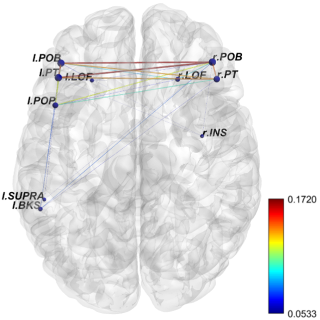
- Investigate the latent variables learnt during model training
  - Output of each graph filter in the graph convolution layer
  - Building blocks $\mathbf{Z}_i$ that generate reconstructed FC graph



- Subgraphs may reveal key insights about SC-to-FC mapping

Numerical tests: Component graphs





- Left: subnetwork of regions in frontal and parietal lobe
  - *Precentral (PRC), Paracentral (PARA)*, motor/sensory functions
  - *Postcentral (POC), Superior Parietal (SP)*, spatial/somatosensory
- Right: subnetwork of regions in Inferior Frontal Gyrus
  - *Parsopercularis (POP), Parsorbitalis (POB), Parstriangularis (PT)*
  - Critically involved in complex brain functions [Greenlee et al'07]

Summary and the road ahead

- Preliminary study of human brain SC-FC relationship
- Reconstruct FC given SC input
  - $\Rightarrow$ GCN-based encoder-decoder model
  - $\Rightarrow$ Learn population patterns of SC-FC mapping
- Latent variables contain vital information
  - $\Rightarrow$ Identify subnetworks contributing to FC formation from SC
- Numerical tests with a large population of HCP subjects
- Envisioned application domains
  - (a) Conduct patient-control comparison
  - (b) Identify potential regions or subnetworks as biomarkers
  - (c) Explore alternative node attributes as graph signals