TUTORIAL: BRAIN CONNECTOME ANALYSIS WITH GRAPH NEURAL NETWORKS

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ABSTRACT

Mapping the connectome of human brains using structural or functional connectivity has become one of the most pervasive paradigms for neuroimaging analysis. Recently, Graph Neural Networks (GNNs) motivated from geometric deep learning have attracted broad interest due to their established power for modeling complex networked data. Despite their superior performance in many fields, there has not yet been a systematic tutorial on practical GNNs for brain network analysis. In this tutorial, we will cover (1) the summarization of brain network construction pipelines for both structural and functional neuroimaging modalities; (2) the modularization of fundamental GNN designs for brain networks and a set of recommendations on general effective recipes based on empirical observations; (3) hands-on instructions on our out-of-box Python package BrainGB, which is available at `https://braingb.us` with models, tutorials, and examples; (4) more advanced GNN designs and training strategies for brain network analysis and future directions. We believe this tutorial can bridge researchers in neuroscience and machine learning/deep learning and offer insights for future research in this novel and promising direction.

***Index Terms*—** Brain network analysis, graph neural networks, deep learning for neuroscience, medical imaging

1. TOPIC OVERVIEW AND EXPECTED LEARNING OUTCOMES

The human brain is at the center of complex neurobiological system that controls behavior and cognition. Brain imaging studies have found that interactions between brain regions play a key role in neural development and disorder analysis [1, 2]. Brain networks, modeled using graph theory, describe the interactions between brain regions. Medical imaging techniques such as MRI are used to scan the brain, which is the most widely used for brain analysis research. Different MRI modalities, like fMRI and DTI, can be used to construct functional and structural brain networks, which describe correlations between brain regions and physical connections between gray matter regions [3], respectively. These connections are valuable resources for understanding the brain [4, 5].

Previous studies on brain network analysis used shallow models based on graph theory [5, 6] and tensor factorization [7, 8] to detect network communities and identify central elements, but these models can be limited to complex brain network structures [9]. In recent years, Graph Neural Networks (GNNs) have attracted broad interest in analyzing graph-structured data [10, 11, 12]. Several pioneering deep models have been devised to predict brain diseases by learning graph structures of brain networks. For instance, [1] propose BrainGNN to analyze fMRI data, where ROI-aware graph convolutional layers and ROI-selection pooling layers are designed for neurological biomarker prediction. [13] design a CNN framework BrainNetCNN composed of edge-to-edge, edge-to-node, and node-to-graph convolutional filters that leverage the topological locality of structural brain networks. However, due to the ethical issue of human-related research, the datasets used are usually not publicly available and the details of imaging preprocessing are not disclosed, rendering the experiments irreproducible for other researchers. Besides, training deep models requires large amounts of labeled data, which is often scarce due to the complexities of neuroimaging data acquisition.

To address these aforementioned problems, recently researchers have widely leveraged different machine-learning techniques for GNN-based brain network analysis, including interpretable model designs [14, 1, 15, 16, 17], multimodality analysis [18, 19], dynamic network analysis [20, 21], generative neural networks [22, 23], resource-limited training [24, 25], etc. In this tutorial, we systematically review and discuss the recent advances in brain network analysis with Graph Neural Networks (GNNs), and provide a hands-on tutorial section for researchers from inter-disciplined areas who are interested but new to the field.

Expected learning outcomes. For both the neuroscience and graph machine learning community, we believe this is an edge-cutting research topic with important scientific impacts and can potentially inspire new understanding or innovative ideas for neural network designs. This tutorial has the potential to have a significant impact on the field of computational neuroscience and deep learning. By providing a comprehensive overview of brain network analysis with Graph Neural Networks (GNNs), it can help researchers, practitioners, and students understand the latest deep geometric learning techniques and use them for brain network analysis. The hands-on sessions and real-world case studies can help the participants apply their newfound knowledge to their research, leading to more efficient verification. Moreover, the tutorial can also foster collaboration and knowledge sharing among participants from different disciplines, leading to innovative approaches for brain network analysis and contributing to the advancement of this field.

2. RELEVANCE TO ISBI COMMUNITY

Brain network analysis is a well-established topic in the ISBI community, e.g., the workshop hosted at ISBI 2022 by Maria Giulia Preti from EPFL, Switzerland, and Thomas Bolton discusses how Graph Signal Processing Opens New Perspectives for Human Brain Imaging. However, our knowledge indicates that no existing tutorial covers brain network analysis with graph neural networks. Our workshop aims to provide a fresh perspective by combining advanced geometric deep learning algorithms with brain network analysis.

Related workshops on brain network analysis include: (1) Eduarda Gervini Zampieri Centeno, Giulia Moreni, Chris Vriend, Linda Douw, and Fernando Antônio Nóbrega Santos, A hands-on tutorial on network and topological neuroscience, at Brain Structure and Function (Brain Struct Funct) 2021; (2) Bernard Ng, Sanmi Koyejo, and Sandro Vega Pons, Brain Network Analysis, at Pattern Recognition in Neuroimaging (PRNI) 2016; (3) Danielle S. Bassett, Brain network analysis: a practical tutorial at Brain 2016. Besides, there is a tutorial on more general geometric deep learning on imaging data: Jelmer Wolterink, Angelica I Aviles-Rivero, and Erik Bekkers, GeoMedIA: Geometric Deep Learning in Medical Image Analysis, at MICCAI 2022, which covers neural networks for learning on point clouds, graphs, and meshes. Although these listed tutorials cover brain network analysis in both theoretical and practical manners, none of them focus on the recent emerging graph neural network and stress the issue of insufficient training data for deep models.

3. CONTENT DETAILS

- **Introduction and Overview**
  In this section, we will introduce the background knowledge about brain network data and Graph

Neural Networks (GNNs). Afterward, we will discuss the challenges of effectively adopting GNNs for brain network analysis:
  - Brain Network Analysis [26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36]
  - Graph Neural Networks [10, 37, 11]
  - Challenges of GNNs for Brain Network Analysis [1, 14, 38, 39]
- **Brain Network Construction Demonstration**
  In this section, we will discuss the diverse modalities of neuro-imaging [40] and demonstrate the main procedures to construct brain networks that model different connectivity (i.e., functional or structural) from popular modalities of raw neuro-imaging data [41, 29, 30, 42]:
  - Functional Brain Network [43, 43, 44]
  - Structural Brain Network [45, 46]
- **Fundamental GNN Design for Brain Network Analysis**
  In this section, we decompose the design space for basic message-passing GNN design into four modules and explain different possible variants under each dimension, together with the empirical insights on general recipes for effective GNN designs on brain networks, which is all integrated into our BrainGB [14] package and serve as a starting point for further studies:
  - Node Feature Construction
  - Message Passing Mechanisms
  - Attention-Enhanced Message Passing
  - Pooling Strategies
- **BrainGB Package Hands-on**
  In this section, we will provide hands-on instructions on the out-of-box package BrainGB on example brain network datasets. The instruction materials are available at `https://braingb.us`.
- **Advanced GNN Designs for Brain Network Analysis**
  In this section, we cover a series of advanced GNN designs and training strategies for brain network analysis, including
  - GNN for Multimodality Brain Networks [18, 19]
  - Interpretable GNN for Brain Networks [1, 15, 16, 17]
  - GNN for Dynamic Brain Networks [20, 21, 47]
  - Generative GNN for Brain Networks [22, 23]
  - Resource-limited GNN Training for Brain Networks [24, 25]
- **Discussions and Future Directions**
  At last, we will elucidate open challenges and future directions from the following perspectives:
  - Neurology-driven GNN design
  - Pre-training and transfer learning of GNNs for Brain Networks

4. TARGET AUDIENCE

The target audience for this tutorial includes researchers, engineers, or graduate students in the field of computational neuroscience, brain network analysis, or machine learning as well as those who are new to and interested in this topic. The audience is expected to have a basic understanding of machine learning and deep learning. Prior knowledge of Graph Neural Networks (GNNs), graph theory, and neuroimaging data analysis would be beneficial but not essential, as the tutorial aims to provide an overview of the techniques and their applications in brain network analysis. Some experience with programming and popular deep learning frameworks such as PyTorch would also be helpful in following the hands-on section and understanding the implementation details.

5. FORMAT AND COURSE PACKS

During the tutorial, we plan to incorporate interactive activities such as group discussions and question-and-answer sessions, along with lectures to keep the audience engaged and involved in the learning process. These activities will provide opportunities for the audience to share their own experiences, ask questions, and discuss real-life scenarios related to the topic. In the hands-on and demonstration sections, we will provide step-by-step instructions on our out-of-box pip installable

Python package BrainGB on example brain network datasets. We will encourage the audience to bring their laptops to participate in this session, where they can apply what they have learned and gain practical experience. We also plan to use visual aids, such as slides and diagrams, to support the lecture content and make the information easier to understand. We will post all the materials of this tutorial, including tutorial documents, presentation slides, and speaker recorders on our hosted website for post-tutorial reviews.

6. PLANED SPEAKERS AND EXPERTISE

Hejie Cui is a Ph.D. candidate in Computer Science at Emory University. Her research interests span interpretable learning of graphs from multimodality data, as well as their applications in neuroscience and healthcare.

Xuan Kan is a Ph.D. candidate in Computer Science at Emory University, under the joint supervision of Prof. Carl Yang and Prof. Ying Guo. His research focuses on designing learning algorithms that are efficient and interpretable for fMRI data.

Xiaoxiao Li is an Assistant Professor in the Electrical and Computer Engineering Department, an Associate Member in the Computer Science Department, and a member of Biomedical Imaging and Artificial Intelligence at the University of British Columbia, leading the Trusted and Efficient AI Lab. She is an adjunct Assistant Professor at Yale University. Her current research lies in machine learning and its application to healthcare.

Ying Guo is a Professor in the Department of Biostatistics and Bioinformatics and Neuroscience Program at Emory University. She is the Director of the Center for Biomedical Imaging Statistics (CBIS). Her research focuses on developing analytical methods for neuroimaging and mental health studies. She is a Fellow of American Statistical Association (ASA) and Chair-Elect of the ASA Statistics in Imaging Section and Standing Member of NIH Emerging Imaging Technologies in Neuroscience (EITN).

Lifang He is an Assistant Professor in the Department of Computer Science and Engineering at Lehigh University. Her research is focused on developing machine learning methods for biology and biomedicine, and ultimately furthering the understanding of disease pathologies and improvement of treatment strategies. Dr. He has worked extensively on brain connectome analysis and has a long history of successful interdisciplinary collaborations with researchers in neuroscience and biology.

Liang Zhan is an Associate Professor in the Department of Electrical & Computer Engineering and Bioengineering at the University of Pittsburgh, where he serves as the associate director of the Pittsburgh Center for Artificial Intelligence Innovation in Medical Imaging (CAIIMI). His research areas include brain connectomics and data mining as well as clinical/translational research on brain diseases such as Alzheimer's disease.

Carl Yang is an Assistant Professor in Emory University. He received his Ph.D. in Computer Science at UIUC. His research interests span graph data mining and machine learning with applications in neuroscience and healthcare. He is a recipient of the Dissertation Completion Fellowship of UIUC in 2020, the Best Paper Award of ICDM in 2020, the Amazon Research Award in 2022, the Best Paper Award of KDD Health Day in 2022, the Best Paper Award of ML4H in 2022 and the NIH K25 Award in 2023.

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