Honors Thesis Proposal

For

Joint Graphical Lasso and Deep Learning Methods for Dynamic Brain Connectome Prediction

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ABSTRACT

The advent of Connectomics has given rise to an array of efforts dedicated towards furthering our understanding of the brain. In general, these investigations are concerned with discovering patterns in neural connectivity; hoping to uncover model pathways of neurological behavior. Utilizing the mainstay of Connectomics, brain connectomes, there exists an opportunity to expose current abstractions that induce collective comprehensions surrounding the brain. Within this scope, our intent seeks to establish a joint method; combining the frameworks of Graphical Lasso and Deep Learning architectures for dynamic hierachical connectome prediction. This entails formulation of an algorithmic model of neural connectivity that not only considers the pair-wise relations of neurons, but intuitively takes into account the hierachical structure of organized neural systems i.e. the brain. Specific to the purview of computational viability, previous experimentation suggests these frameworks yield measurable improvements in their capacity to interpret neural data as necessary; providing ample justification of the aforementioned proposal. In practice however, several considerations exist requisite to the efforts at hand. Of these, a peculiar focus on maintaining scalability and temporal structure throughout deems critical; as interpretation of high-dimensional data while abstaining from effects of temporal warping serve as kernels to our schema. Further developments within this framework aim to maintain efficacies throughout each task within our joint method; feeding time-series activation data of neurons and approximating higher-order structures of neural connectivity in a computationally efficient manner. Contingent on our success, the findings provide grounds for an enhancement in further inspections of neurophysiological phenomena.

PART 1: INTRODUCTION AND BACKGROUND

1.1 OVERVIEW

This proposal details how a joint approach to predicting neural causality (if two neurons are paired) can arise from merging Graphical Lasso and a novel Deep Learning architecture. With demonstrable success, the architecture has shown to perform exceedingly well on the task of predicting neural causality [1]. Likewise, Graphical Lasso (more specifically Structural Graphical Lasso) has had its share of utility in the realm of inferring brain connectivity from the Allen Developing Mouse Brain Atlas [2,3]. Acting as a regularization agent, the aim is to integrate Graphical Lasso and this Deep Learning architecture in order to relegate key feature selection – providing a means to increase prediction accuracies.

The scope of this problem generally nests itself within the supervised learning paradigm. As will be mentioned in following sections, a series of ground-truth values for neuron pairs are provided – by which a model can be learned to identify features unique to pairs of neurons which are causally connected. This data, as part of a larger effort hosted during the ChaLearn Neural Connectomics Challenge [4], provides the capability for a multi-layered yet tractable solution.

1.2 NEUROSCIENCE

Though not the center-piece of this project, a formal understanding of several key concepts greatly helps solidify the intuitions to the approach measured in this project. Of these ideas, one which can go no further without address is neural causality. This phenomena describes how neurons maintain a characteristic of causality with other neurons – that is to say, when one neuron fires it affects the

likelihood of another neuron firing [5]. This dependency provides an interesting vantage point by which macroscopic models of brain activity can be formed: namely brain connectomes. A fairly recent endeavor by the Human Connectome Project led by the WU-Minn Consortium [6] spurred interest in ways to effectively generate these connectomes – mappings of neural connectivity in the brain.

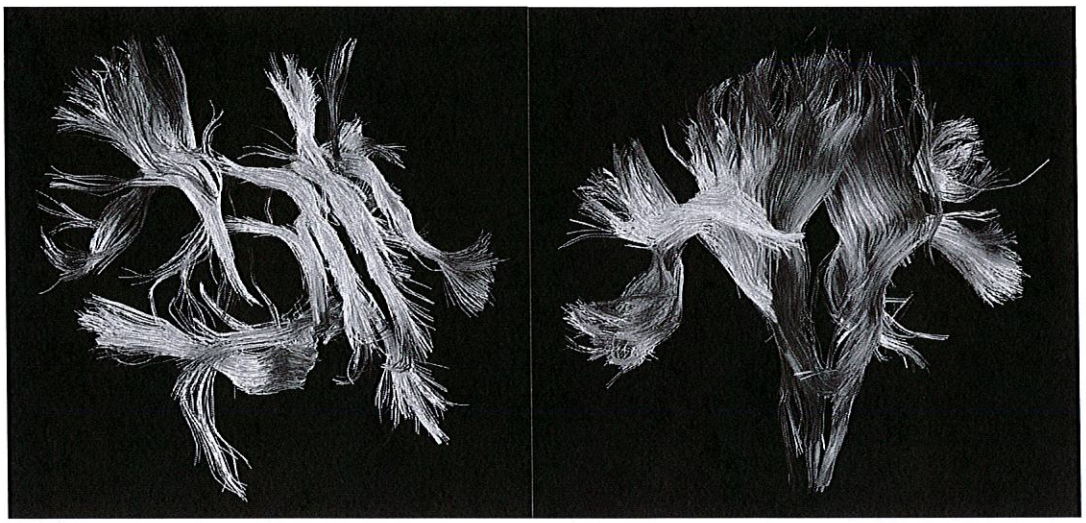

Figure 1: Example Brain Connectomes generated by WU-Minn Consortium [7]

The problem can be challenging however due to the sheer amount of connections that any given neuron has (up to thousands). Nonetheless the approach detailed in following section focuses on the smaller sub-task of detecting causality between just two neurons.

1.2.1 NEUROPATHOLOGY

Of particular interest to these brain connectomes, as shown in figure 1, are those who study neuropathological diseases like epilepsy, autism, and Alzheimer's. Often the case for diseased patients are that the functional connectivity between their brain regions is fundamentally different from healthy counterparts [8, 9]. Utilization of generated brain connectomes offer a new avenue by which these diseases can be studied and effectively researched. Additionally, a powerful visualization of these core differences in brain activity can be readily distinguished among healthy and diseased patients. Though

not the focus of this project, it is relevant to note the future utility and critical application of the proposed work in generating brain connectomes.

1.3 MACHINE LEARNING

The core proponents of the algorithm developed in this work employ a range of tools in Machine Learning. Of these, the majority fall under the realm of supervised learning – engaging with a series of methods in deep learning and artificial neural networks. The gist of these procedures involve a training process with access to ground-truth values (key distinction to the unsupervised paradigm). In this project it comes in the form of a test set of neuron pairs by which their causality is readily known.

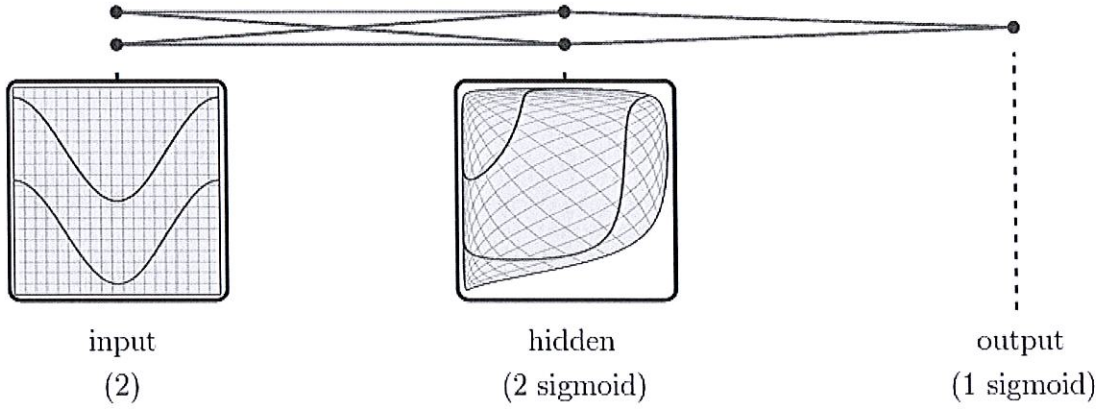

Figure 2: Visualization of Neural Network Classification [12]

Within the supervised scope, there are generally two problem types of interest to Machine Learning researchers: regression and classification. Regression is the process by which future approximations (generally scalar) are made based on previous trends e.g. stock market prediction [10]. Of specific interest to this effort is classification, where new observations are identified into a set of categories to which they likely belong e.g. distinguishing images of cats and dogs. [11] The process as visualized in figure 2, shows how (in the case of neural networks) a solution space is transformed in successive

layers until it can readily find a line, plane, or hyperplane (dependent on dimensionality of data) by which categories can be separated.

Neural networks are versatile in their capabilities and as will be discussed in later sections, a variety of them exist: convolutional, recurrent, and their "deep" derivatives. Each with distinct structural differences, the general form is again shown by figure 2, with an input layer succeeded by a varied amount of hidden layers that ultimately feed to an output layer [12]. As mentioned before, these layers serve to transform the data into a linearly separable space, each layer encoding different features of the data. Though the simple model of classification in figure 2 provides too crude of a generalization to the classification process (with regards to this proposal, it is far too simple) it does provide a great measure by which to understand the core principles underlying this project.

PART 2: LITERATURE REVIEW

2.1 RELEVANT ASPECTS TO BE REVIEWED

To better understand the intuitions behind more advanced concepts utilized in this project, a review of core literature is pertinent. This review will focus predominantly on the two papers by which the "joint" aspect of this endeavor received its name: previous work on a Deep Learning Architecture for Dynamic Brain Connectome Prediction [1] and Graphical Lasso [2]. A deeper look at the contents of these papers will provide a clearer understanding of their inherent benefits and compatibility within a common framework.

2.1.1 DEEP LEARNING ARCHITECTURE FOR BRAIN CONNECTOME PREDICTION

Presented in this paper [1] is an algorithm by which an input of spiking sequences of neurons can be readily classified as causally connected or not. The key contributions are a dynamically programmed layer, working in tandem with recurrent and convolutional neural nets, to determine the alignment between neuronal activations of pair-wise combinations of neurons [1]. Using the same dataset proposed for this study [4], the deep learning architecture (as depicted in figure 3), was tested along several other metric algorithms: including Granger Causality, Partial Correlation Statistics, Generalized Transfer Entropy, and others. Of critical importance is its performance relative to the winner of the connectivity prediction challenge by which the data was provided – where this architecture bested the winner's accuracy by a measurable margin. The success of this model provided a strong platform by which to expand on the architecture, in an attempt to further push detection accuracy: the main aim of this project.

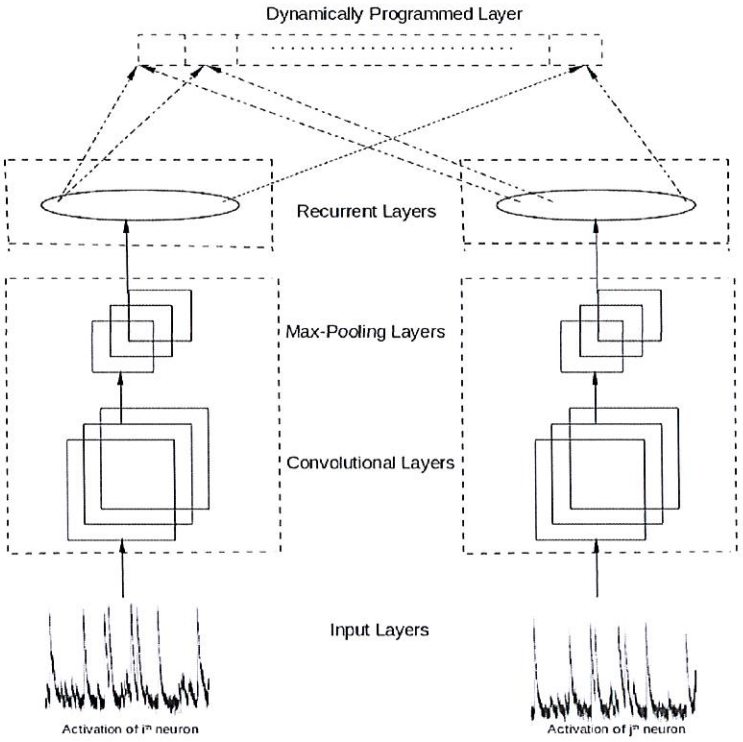

Figure 3: Depiction of Deep Learning Architecture

2.1.1.1 ARCHITECTURE BREAKDOWN

The architecture consists of a series of layers, each feeding to the next as shown in figure 3. First, two neural spiking sequences are received, which are first processed at a convolutional layer. This layer serves to initially prime and exploit the temporal structure of the input, extracting salient patterns from the neural spiking sequences. At this point, the data can be sent to a max-pooling layer that down-samples the initial sequence to provide a more comact, but still robust representation of the input sequences. This step is crucial in reducing the processing cost of analyzing time-series data as it essentially strips away initial information in a way that is largely invariant to any warping of temporal structure – speeding up computation on the sequences. After max-pooling, the data is sent to another temporal processing unit: the recurrent layer that learns the key features via backpropagation through time, which encodes valuable features necessary in determining neural causality. Once the temporal

structure is effectively encoded, a dynamically programmed layer can compare the two input sequences by which the output prediction layer effectively classifies the pair-wise neuron combination as causally connected or not. This provides a quick generalization of the architecture's classification process.

2.1.2 GRAPHICAL LASSO FOR LEARNING MOUSE BRAIN CONNECTIVITY

This effort provided a method towards generating a graphical model that can effectively perform inference on mouse brain networks. Its primary contribution, and the one of most interest to this effort, is the formulation of Graphical Lasso regularization procedure [2]. Motivated by the hierarchical nature of the brain, this regularization method provides a way to screen large numbers of features present in neural data and identify those by which classification deems them most relevant. Hence forth, this ability to distinguish between the pertinent features used in training or building a model for neural causality prediction provides an interesting opportunity to attempt a segue outside of graphical models – towards a deep learning implementation.

2.2 SUMMARY

Both the papers reviewed provided an approach to analyzing connectivity of neural data. From the results generated by the deep learning architecture, it can be reasonably said that a proper baseline method is available by which to experiment with modifications via regularization. For this purpose, the literature reviewed on graphical lasso provides the opportunity to fuse the approaches. Combining the substantial performance of the deep learning architecture with the feature-selection of graphical lasso could potentially further improve the performance of the base deep architecture: the primary goal of this project.

PART 3: METHODOLOGY

The following subsections depict the process by which this project aims to implement and test the joint method proposed. A hypothesis provides an expectation of the results, and the contributions listed describe the goals of this effort. Lastly, the process and methods used throughout will be described.

3.1 HYPOTHESIS

A deep learning architecture bolstered by graphical lasso regularization can provide improvements to the prediction of neural causality via improved feature selection.

3.2 CONTRIBUTIONS

The following are the proposed contributions of this effort:

- A joint graphical lasso and deep learning method for dynamic brain connectome prediction.
- A tool by which neural causality can be accurately predicted

3.3 METHODS

This study will be conducted using a MATLAB implementation of the joint method described. Once finished, the implementation will be trained and then tested alongside the performance metrics specified in [1], to definitively assess whether an improvement was made by incorporation of graphical lasso. Concurrent with the original approach, the data to be used will continue to be the ChaLearn connectomics challenge test set.

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