

Connectomics: Neural Structure Reconstruction from Fluorescence Imaging of Neural Activity

Project Proposal

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Abstract: Understanding the topology underlying neural connections and the associated changes induced by defects is often deemed a promising approach to deciphering the puzzle of neuro-pathologies, eg. epilepsy, Alzheimer's disease.

In this work, we would like to reconstruct the network structure of the brain from time-series activity of the neurons. Since the connections are directed in nature, the fundamental obstacle the task entails is that of inferring statistical causality from time-series data.

Keywords: Neural Structure • Fluorescence Imaging • Time Series • Causality • Statistics

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1. Motivation

The field of Connectomics is concerned with the study and construction of a comprehensive map of an organism's neural connections in the brain. Understanding the topology underlying the neurons promises to be a step forward to unravelling the working of the brain and shed some light on it's learning capabilities. The study of how the network structure is modified by diseases could catalyse the research on neuro-pathologies, eg. epilepsy, Alzheimer's disease. However, the traditional methods of axonal tracing do not scale enough of be practical value; since the number of neurons is typically in billions, with each node having about ten thousand connections. A very cost-intensive and tiresome method is that of electron microscopy, but it does not share the benefits of automation, requiring a lot of human effort. Moreover, this method can't be done in vivo.

2. Background

The activation of a neuron can potentially lead to activation of the neurons it is connected to through the network topology. The signal, encoding the activation, transmitted from one neuron to another is carried through chemicals

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called **neuro-transmitters**. The neuro-transmitters are only released if the action potential is sufficiently high, which in turn is controlled by the influx of calcium ions. If the (traditionally dissected) neural tissue is injected with fluorescence dye labelled calcium, the accumulation of calcium ions, and hence the neural activity, can be observed by relatively inexpensive fluorescence imaging techniques.

3. The Challenge

We would like to tackle the challenge of network structure discovery by observing the dynamics of neural activity behaviour captured by the imaging techniques.

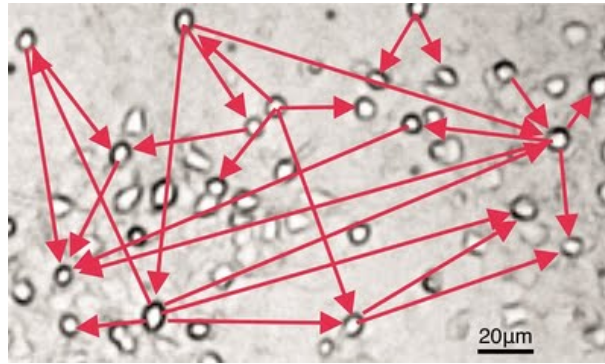


Figure 1. Network reconstruction of in vitro neural cultures imaged with fluorescent calcium imaging [8]. The white dots are real neuron cell bodies. The red arrows are effective connections recovered computationally from videos of neural activity.[10]

The task of reverse engineering neural structure topology from the activity data seems a very promising venture to by-pass the practical in-feasibilities that bind the current methods. The goal of this challenge is to infer directed connections between neurons from time-series patterns of neural activity. Such a directed graph may be interpreted as a causal network. Further, neurons have complex temporal patterns of activity. The challenge can therefore be viewed as that of causal structure reconstruction from time series data[10].

4. Methodology

The authors completely agree with the above stated view of looking at this as that of recovering causal structure from time-series data. In this section, we describe the possible approaches and the ones popularized by the literature.

There have been 2 major categories of methods in the literature: conditional independence testing[1] championed by Judea Pearl and Granger time-series based causality testing[2]. Since we have a time-series data, we consider the second method. It is interesting to note that on the very same work, Clive Granger was awarded the Nobel

Prize in economics, citing his contributions to econometrics.

The basic idea behind Granger causality test is to see if the observed time series yields a better fit in one direction over another; i.e. to fit various predictive models upon $A(\text{present time})$ and $B(\text{present time})$ as a function of $A(\text{past times})$ and $B(\text{past times})$. Clues are obtained if A can be better predicted from past values of A and B rather than from A itself but B cannot be predicted from past values of A and B rather than from B itself. In such a case, we infer that " A implies B " is more likely.

The literature surrounding the area is rich with alternatives and adaptations of Granger causality. One could look at the data in the frequency domain[3] instead of the time domain. Since the frequency at which the data is sampled could be low leading to low-resolution time series, in such cases, it becomes necessary to incorporate current values[4] of A and B into the set of parameters to predict each other. A particularly innovative approach is of that of looking at non-linear fits instead of simple auto-regressive linear models for time series predictions. One much measure involves looking at Transfer Entropy[5], which the authors see as a certain inclusion in their predictive model.

Another perspective is to start with the space of all possible topologies and then, try to fit ones which explain (generative models) the observed data well. Among the popular approaches are Dynamic Causal Modelling[6] using probabilistic graphical models and regularization based lasso methods[7] for regression.

Yet another problem which plagues the current task, which is also common to statistical causality, is that of confounding; i.e. a common factor being the cause of two effects, so that one may confuse one effect as the cause of another. One idea to counter this is to condition the probabilities on the near-by neural activity[8][9]. Another is to look at information theoretic constructs which are not symmetric when viewed from cause-effect and effect-cause angles.

5. Notes on Data-set

The challenge is currently hosted on Kaggle by the organizers[10]. The data set consists of 20ms time-series data set of neural activity of 1000 neurons. Hence, the output size is a million entries, a prediction for each link. The data is synthetically generated, since establishing the ground truth for such networks is very expensive. The training data has been provided under varying settings of sub-normal and super-active neural activity.

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