Inferring Functional Connectivity of Neurons From Spiking Activity

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Abstract

Our project aims to model the functional connectivity of neuronal microcircuits. On this scale, we are concerned with how the activity of each individual neuron relates to the other neurons in the population. Recent innovations, including the use of calcium indicator dyes or multi-electrode arrays (MEA), allow researchers to collect individual spiking activities of large groups of neighboring neurons, supplying the data to address the fundamental problem of connectivity. We will develop a model to infer a neural connectivity matrix given spike train data that improves and builds on prior research efforts. With a better understanding of the functional patterns of neural activity at the cellular level, we can begin to decode the building blocks of neural computation.

1 Introduction

As we learn more and more about the workings of the neuron and of specialized brain regions, the question increasingly becomes, how do these pieces sum to a whole? How do the patterns of connectivity give rise to vision, memory, motor function, and so on? Currently, a broad picture of the circuitry, or graphical connectivity, of the brain does not exist, but several projects are underway to organize the solution of this problem [8, 3]. Efforts to examine connectivity of the brain focus on scales ranging from brain regions each comprised of hundreds of millions of cells down to microcircuits of only a few cells. Further, some of these projects address structural connectivity and others functional connectivity [7, 6, 12, 4, 2].

In this project, we will model the functional connectivity of microcircuits: how electrical activity in one neuron influences activities in other neurons. Importantly, functional connectivity does not always imply anatomical connectivity; it only implies that some set of neurons fire together in correlation. Without anatomical corroboration, these jointly firing neurons may have a common input or be linked in a chain, rather than lie physically adjacent. Providing experimental evidence of predicted connectivity between pairs of neurons in the circuit is not in the scope of this project; however, we intend to use real calcium imaging and multi-electrode array (MEA) data for our analysis, and expect to see results consistent with the neural connectivity literature. Some measures of this consistency would be that each neuron obeys Dales law, i.e. they are either purely excitatory or inhibitory, and that connectivity is sparse. With simulated data, we will also be able to see how sensitive the connectivity inference is to various parameter structures and decide whether these sensitivities or lack thereof are biologically reasonable.

Several strategies have already been employed to infer the functional connectivity of microcircuits from calcium imaging and MEA data [5, 14, 1]. Of special interest to us and our approach are two recent Bayesian approaches. In [10], a pattern-growth algorithm is used to find repeated episodes of activity. These patterns define mutual information between neurons which they summarize in a dynamic Bayesian network. While their methodology presents a contribution to the study of Bayesian networks, one limitation of this work in inferring the connectivity of microcircuits is that it only

discovers relationships of excitation. In [9], network activity is modeled in terms of a collection of coupled hidden Markov chains, with each chain corresponding to a single neuron in the network and the coupling between the chains reflecting the networks connectivity matrix. To make computation feasible they used a blockwise-Gibbs sampling method and took advantage of the parallel computing possibilities when implementing their expectation-maximization algorithm. Although the work to date has done much to address the problem of functional neural connectivity, there are still improvements to be made to current models. For example, current models do not address unobserved inputs to the system. By developing a new model, we can address these issues as well as explore potentially new ways of inferring functional connectivity on the cellular scale.

It is not yet clear how microcircuits code neural computations, nor how they might generalize across brain regions or individuals, but by uncovering the patterns of activity between neurons we begin to decode these computational processes.

2 Methods

TBD.

3 Experiments

TBD.

4 Conclusion

We will develop a model to infer a neural connectivity matrix given spike train data (either continuous measurements, such as fluorescence levels, or discrete spikes) that improves and builds on prior research efforts. As ground truth data is limited in this domain, we will primarily measure performance using the same simulation processes and metrics used in the source papers for our model. Specifically, we expect our model to accurately retrieve the connectivity parameters used to generate the simulated data.

Further, since our team has access to limited lab data of spike trains, we will also compare our model against existing models on real data and expect our model to outperform on real data as well. A potential metric for performance in this regime may come from the few experiments done, where dozens of cells are voltage clamped simultaneously, and functional connections are accurately teased out through direct measurements of post synaptic currents. Certain graphical features have been inferred about the entire microcircuit from these limited electrophysiological data, such as the existence of scale-free, small world networks with certain two, three, and four cell motifs overrepresented as compared to a randomly connected network [13, 11]. So in comparison to other models we may expect to validate these graphical features in the analysis of real data.

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