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Day Month Year of submission

Abstract

Abstract content.

Sommario

Contenuto del sommario.

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Introduction

Overview

A fundamental but unsolved problem in neuroscience is understanding the functioning of neurons and neuronal networks in processing sensory information, generating locomotion, and mediating learning and memory. The investigation of the structure and function of the nervous system can be dated back to the nineteenth century with the invention of the technique of silver impregnation by Camillo Golgi in 1873, which allowed the visualization of individual neurons (Drouin *et al.*, 2015). The technique initiated the study of the microscopic anatomy of the nervous system, and the investigation of how neurons organize to form the brain. Ever since there has been a significant research effort both to discover the cellular properties of the nervous system, and to characterize behaviors and correlate them with activity imaged in different regions of the brain. However, many scientists recognize that despite the innovative techniques developed to observe and analyze neurons, we are still facing an "explanatory gap" between the understanding of elemental components and the outputs that they produce (Parker, 2006, 2010; Dudai, 2004). That is, we know a lot about the components of the nervous system, but still we have little insight into how these components work together to enable us to think, remember, or behave. One of the reasons of this gap is the availability of a huge quantity of data, but a lack of tools to integrate these data in order to obtain a coherent picture of the brain functioning (Parker, 2010).

The technological developments of the last few decades have opened fundamentally new opportunities to investigate the nervous system. Large neuronal networks can now be visualized using *in vivo* high-resolution imaging techniques, which permit to record the neuronal activity in freely moving animals over long periods of time. In this thesis, we focus on data resulting from the application of the two-photon calcium imaging technique. Calcium ions generate intracellular signals that determine a large variety of functions in all neurons: when a neuron fires, calcium floods the cell and produces a transient spike in its concentration (Grienberger and Konnerth, 2012). By using genetically encoded calcium indicators, which are fluorescent molecules that react when binding to the calcium ions, it is possible to optically measure the level of calcium by analyzing the observed fluorescence trace. However,

extracting these fluorescent calcium traces is just the first step towards the understanding of brain circuits: how to relate the observed pattern of neuronal activity with its output remains an open problem of research.

The analysis of calcium imaging data comprises many stages and has several objectives. The output of this technique is a movie of time-varying fluorescence intensities, and a first complex pre-processing phase deals with the identification of the spatial location of each neuron in the optical field and source extraction. The resulting processed data consist of a fluorescent calcium trace for each observable neuron in the targeted area which, however, is only a proxy of the underlying neuronal activity. Hence further analyses are needed to extract the spike trains (i.e. the series of recorded firing times), and to try to explain how these firing events are linked with the experiment that generated that particular pattern of activity.

Main contributions of the thesis

Chapter 1

Modeling of calcium imaging data

1.1 Overview of calcium imaging data

Calcium ions generate intracellular signals that control key functions in all types of neurons. The development of techniques that enable the visualization and quantitative estimation of the intracellular calcium signals have thus greatly enhanced the investigation of neuronal functioning (Grienberger and Konnerth, 2012). At rest, most neurons have an intracellular calcium concentration of about 100 nm; however, during electrical activity, the concentration can rise transiently up to levels around 1000 nm (Berridge *et al.*, 2000).

1.1.1 Allen Brain Observatory data

1.2 A brief review of some Bayesian nonparametric models

Chapter 2

Efficient posterior sampling for Bayesian log-linear models

2.1 Algorithm

Chapter 3

Bayesian nonparametric analysis for partially exchangeable single-neuron data

3.1 Model specification

3.2 Posterior computation

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