論文の内容の要旨

論文題目　Log-linear models for the analysis of neural activities in complex settings

（複雑環境下での神経活動を解析するための対数線形モデル）

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This thesis provides theoretical and technical advancements for the statistical analysis of neuronal data. More specifically, we provide new log-linear models of neural activity and use them to address two neuroscientific questions: (1) how do we describe the structure of synchronized cortical activities recorded over multiple electrodes? And (2) how do the responses of single neurons in the caudate nucleus of free-behaving monkeys represent reward and social context information during a social task?

Chapter 1 introduces the theme for this thesis. An ultimate goal of neuroscience is to explain how complex behaviors are generated by complex patterns of neuronal activity in the brain. To investigate a given brain function, traditional neurophysiological studies have laboriously recorded the activity of single neurons during carefully controlled behavioral conditions. Although successful in mapping neuronal functions over several anatomical regions of the brain, this reductionist approach has important limitations: (1) it does not directly explain how networks of neurons function as a whole; and (2) it prevents the investigation of a broad range of complex, natural animal behaviors. Converging technologies have recently loosened these limitations by enabling the simultaneous recording of large-scale neuronal data and detailed behavioral data of free-behaving animals, thus enabling holistic approaches for investigating neuroscientific questions. This thesis addresses the challenges for the statistical analysis of neuronal data in holistic investigations by proposing and validating log-linear models of neuronal activity in two neuroscientific studies.

We provide in Chapter 2 the research background for each study and the general theoretical framework for the thesis. The first study addresses the statistical analysis of large-scale neuronal data, and we review accumulating evidence indicating the functional importance of synchronized activity across multiple neural elements. We highlight the need to find simplified models of synchronized activity for an efficient analysis of large-scale datasets. The second study concerns the analysis of neuronal responses recorded from unrestrained animals. We review studies that have applied log-linear modeling on the recorded neuronal responses during an animal's unrestrained behavior, in order to understand how different aspects of the behavior were encoded in the neuronal activity. We note the potential for applying the free-behavior paradigm together with log-linear modeling to explore the neural basis for the social behavior of animals.

In Chapter 3, we explain how synchronized activity can be theoretically described in terms of neural interactions. Different assumptions about the underlying interactions yield different models, and a hitherto popular log-linear model – the pairwise model – assumed that no interactions involving more than two neural elements needed to be considered – i.e. only first and second-order (pairwise) interactions were necessary to explain the activity. Here we demonstrate, through statistical analyses of spontaneous activity recorded from cortical cultures, that a hierarchical log-linear model provides a better description of synchronized neural states than the pairwise model. The hierarchical model assumes a hierarchy of functional elements – electrodes and clusters of electrodes – and pairwise interactions among the functional elements at each level of the hierarchy. Due to this hierarchical structure, our model is able to capture significant higher-order neural interactions which had been previously neglected by the pairwise model. Thus, our hierarchical log-linear model makes a significant theoretical contribution for the statistical modeling of synchronized neural activity.

We demonstrate in Chapter 4 that a class of log-linear models known as the generalized linear model (GLM) can be used to analyze the neuronal responses in a social experiment with free-behaving monkeys. The purpose of the experiment was to investigate the activity of single neurons in a brain area called the caudate nucleus (CD) in relation to both food rewards and the context of social dominance or submission during a competitive task. Because the monkeys freely moved their upper body during the experiment, it was necessary to dissociate the modulatory components of the external covariates – the motor behavior, the rewards, and the social context – in the neural responses. The GLM dissociated the components and identified CD neurons with significant modulation by social context and / or rewards. Furthermore, it revealed that the information about rewards and social context were independently encoded across the population of CD neurons. Therefore, our successful application of GLM in a free-behavior social task provides a new statistical approach for relating complex social behaviors to neural responses.

We conclude in Chapter 5 by detailing the contributions of this thesis as a whole, and discussing some directions for future research. This thesis demonstrates the flexibility and potential of the log-linear model for future statistical analyses in holistic investigations of brain functions.