Preface

Effective neural motor prostheses require a method for decoding neural activity representing desired movement. In particular, the accurate reconstruction of a motion signal is necessary for the control of devices such as computer cursors, robots, or a patient's own paralyzed limbs. For such applications, we built a collection of practical mathematical models to describe the relationship between neural activity and hand movement. This thesis is a summary of these statistical methods we developed on the modeling of neural signals in monkey's primary motor cortex and the applications of one of them - the linear Gaussian model to direct neural control performance.

The main content of this thesis consists of six chapters:

Chapter 1 is an introduction to the domain of neural prostheses, especially on the motor cortical aspect. We at first provide a general background, then we clearly describe a summarized framework of neural motor prostheses as well as the related key issues. Recent work in this field is reviewed with brief comments. Furthermore, we present our experimental paradigm and detailed process of neural data extraction where the recordings were made in the arm area of primary motor cortex in awake behaving monkeys using a chronically implanted multi-electrode microarray.

Chapter 2 describes our linear Gaussian approach on the modeling and decoding of neural signals. The developed method is a real-time system that uses Bayesian inference techniques to estimate hand motion from the firing rates of multiple neurons. The inference involves computing the posterior probability of the hand motion conditioned on a sequence of observed firing rates; this is formulated in terms of the product of a *likelihood* and a *prior*. The likelihood term models the probability of firing rates given a particular hand motion. We showed that a linear Gaussian model provided a good approximation to this likelihood and could be readily learned from a small amount of training data. The prior term defines a probabilistic model of hand kinematics and was also taken to be a linear Gaussian model. Decoding was performed using a Kalman filter which gives an efficient recursive method for Bayesian inference when the likelihood and prior are linear and Gaussian. In off-line experiments, the Kalman-filter reconstructions of hand trajectory were more accurate than previously reported results. The resulting decoding algorithm provides a principled probabilistic model of motor-cortical coding, decodes hand motion in real time, provides an estimate of uncertainty, and is straightforward to implement.

Chapter 3 discusses a direct application of the Kalman filter in on-line experiments where we demonstrate closed-loop neural control of cursor motion using the Kalman filter. In this task a monkey moves a cursor on a computer monitor using either a manipulandum or their neural activity recorded with a chronically implanted micro-electrode array. A number of advantages of the Kalman filter were explored during the on-line tasks and we found that the Kalman filter had superior performance to previously reported linear filter methods. While the results suggest the applicability of the Kalman filter for neural prosthesis applications, we observed the decoded cursor position was nosier under brain control as compared with manual control using the manipulandum. To smooth the cursor motion without decreasing accuracy we propose a method that smoothes the neural firing rates. This smoothing method is described and its validity is quantitatively evaluated with recorded data.

In Chapter 4, we extend our approach to a non-Gaussian generalization and present a Switching Kalman Filter Model (SKFM) for the real-time inference of hand kinematics from a population of motor cortical neurons. Firing rates are modeled as a Gaussian mixture where the mean of each Gaussian component is a linear function of hand kinematics. A "hidden state" models the probability of each mixture component and evolves over time in a Markov chain. The model generalizes previous encoding and decoding methods, addresses the non-Gaussian nature of firing rates, and can cope with crudely sorted neural data common in on-line prosthetic applications.

Chapter 5 focuses on the decoding of neural signals by the coupling of spikes and local field potential (LFP) in the discrete center-out reaching task. We explore the fast oscillation (15-33Hz) of LFP and firing patterns of single units in motor cortex with respect to a monkey's hand-movement direction. Our work examined, during the instructed delay period, various approaches to couple the LFP and spikes to the encoding of movement direction by counting the number of spikes per unit time within different phases of fast oscillation of the LFP. We found that the coupled rates within certain phases have higher (though not statistically significant) decoding accuracy than the rates over the whole instructed delay period which was reported in previous work.

Chapter 6 offers conclusions of the thesis as well as descriptions of future work.