A point process approach to identifying and tracking transitions in neural spiking dynamics in the subthalamic nucleus of Parkinson's patients

Xinyi Deng,[1] Emad N. Eskandar,[2,3] and Uri T. Eden[1]

[1]Department of Mathematics and Statistics, Boston University, Boston, MA, USA
[2]Department of Neurosurgery, Massachusetts General Hospital, Boston, MA, USA
[3]Harvard Medical School, Boston, MA, USA

Introduction

- Many methods have been proposed and used to study rhythmic dynamics in continuous-valued recordings.
- As opposed to continuous-valued measurements, statistical estimation and inference procedures for neural spike train data are most appropriately developed based on the theory of point processes.
- Neural spike train data exhibit a wide variety of history dependent behaviors such as refractoriness, bursting, and intrinsic rhythms. The probability of a neuron firing a spike in any time interval is often influenced by many factors occurring simultaneously.
- To address these issues, we propose a state-space point process approach for identifying and tracking changes in rhythmic spiking dynamics.

Methods

- Modeling spikes with a point process conditional intensity function.

$$\lambda(t|H_t) = \lim_{\Delta \to 0} \frac{Pr(\text{spike in } [t, t+\Delta)|H_t)}{\Delta}$$
$$= \exp\left[\beta_0 + \gamma_0 \cdot I_{\text{move}}(t) + \sum_{i=1}^{p} \beta_i \cdot g_i(H_t) + \sum_{i=1}^{p} \gamma_i \cdot g_i(H_t) \cdot I_{\text{move}}(t)\right] \quad (1)$$

- Question 1: Has there been a significant change in rhythmic spiking dynamics?

$$\mathrm{H}_0 : \gamma_i = 0 \text{ for all } i \quad \text{vs.} \quad \mathrm{H}_A : \text{For at least some } i,\ \gamma_i \neq 0 \quad (2)$$

$$\Lambda = -2 \log \frac{L(\lambda(t|H_t)|\mathrm{H}_0)}{L(\lambda(t|H_t)|\mathrm{H}_A)} = -2 \log L(\lambda(t|H_t)|\mathrm{H}_0) + 2 \log L(\lambda(t|H_t)|\mathrm{H}_A) \quad (3)$$

Perform the hypothesis test, where Λ has an asymptotic $\chi^2_{(p+1)}$ distribution.

- Question 2: What is the time course of the dynamic changes in rhythmic spiking structure?
Allow the model parameters related to history to change smoothly and estimate their evolution using a point process filtering and smoothing algorithm.
The **model**:

$$\log \lambda(t|H_t) = \beta_{0,t} + \sum_{i=1}^{p} \beta_{i,t} \cdot g_i(H_t). \quad (4)$$

One step prediction:

$$\theta_{t|t-1} = \theta_{t-1|t-1} \quad (5)$$
$$W_{t|t-1} = W_{t-1|t-1} + \Sigma \quad (6)$$

The **filter**:

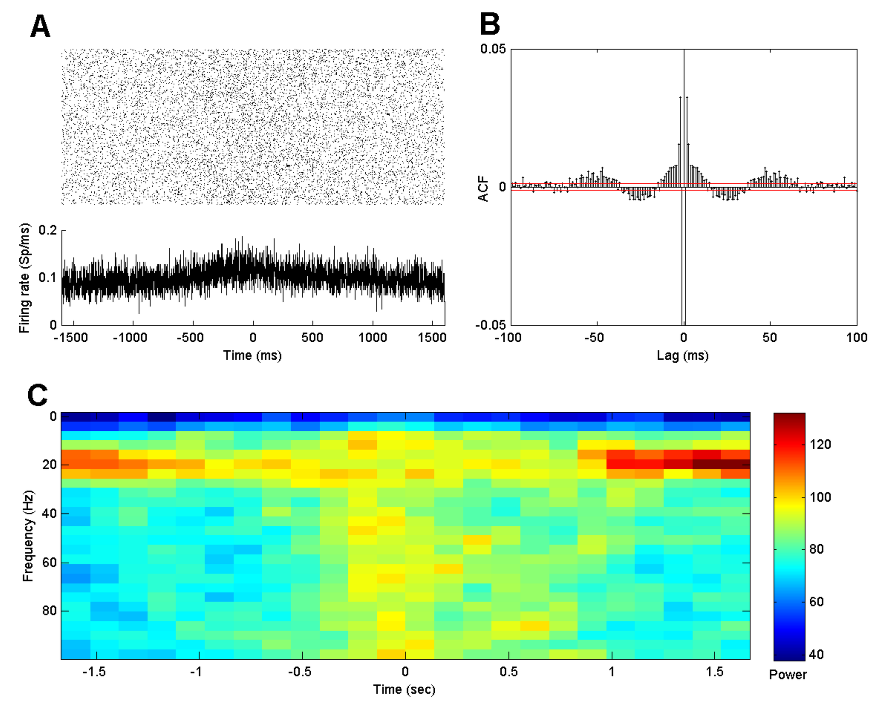
$$W_{t|t} = \left[W_{t|t-1}^{-1} + \frac{\partial^2 \log \lambda}{\partial\theta\partial\theta^T}(\Delta N_t - \lambda_t \Delta t) + \left(\frac{\partial \log \lambda}{\partial \theta}\right)^T \lambda_t \Delta t \left(\frac{\partial \log \lambda}{\partial \theta}\right)\Big|_{\theta_{t|t-1}}\right]^{-1} \quad (7)$$
$$\theta_{t|t} = \theta_{t|t-1} + W_{t|t} \cdot \frac{\partial \log \lambda}{\partial \theta}(\Delta N_t - \lambda_t \Delta t) \quad (8)$$

The **smoother**:

$$\theta_{t|T} = \theta_{t|t} + W_{t|t} W_{t+1|t}^{-1}(\theta_{t+1|T} - \theta_{t+1|t}) \quad (9)$$
$$W_{t|T} = W_{t|t} + W_{t|t} W_{t+1|t}^{-1}(W_{t+1|T} - W_{t+1|t}) W_{t+1|t}^{-1} W_{t|t} \quad (10)$$

Data Visualization and Descriptive Analysis

STN Data

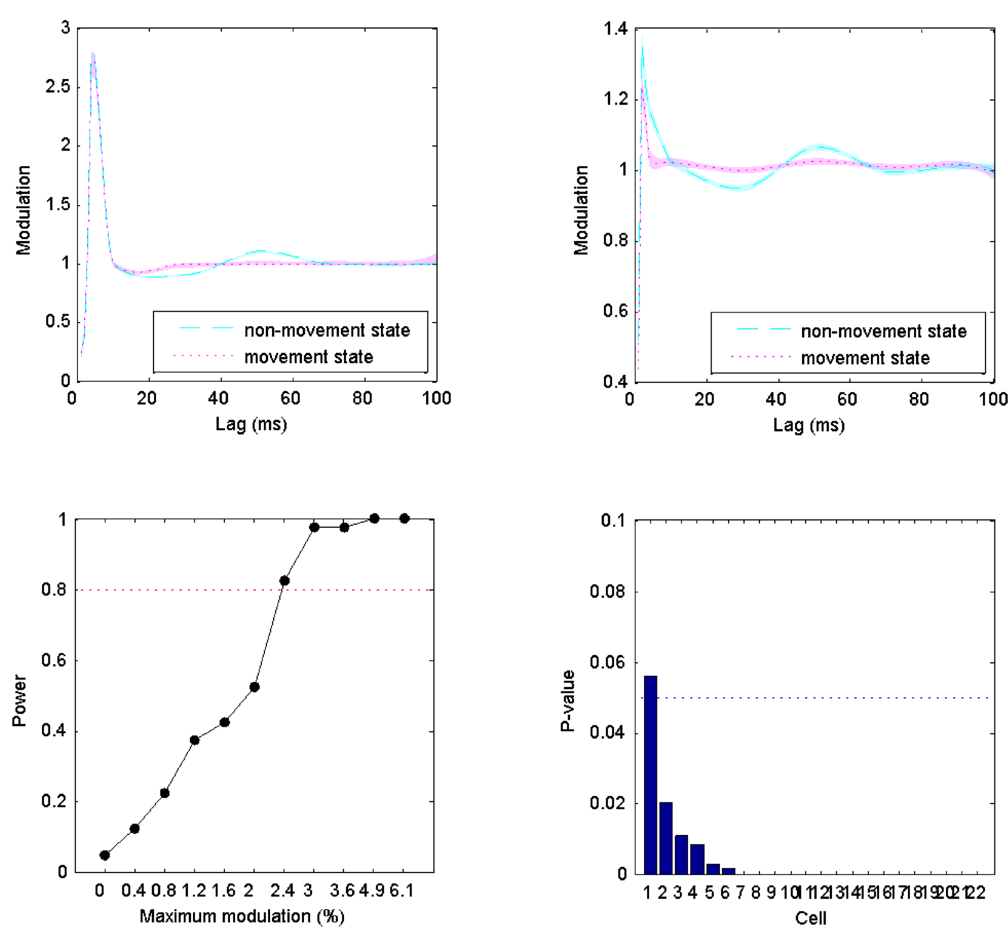


- Single neurons in the subthalamic nucleus (STN) of patients undergoing surgery for the treatment of Parkinson's disease.
- Patients viewed a computer monitor and used a contralaterally mounted joystick to perform a hand movement task.
- Time 0 represents movement onset.

Identifying Significant Changes in Spiking Dynamics

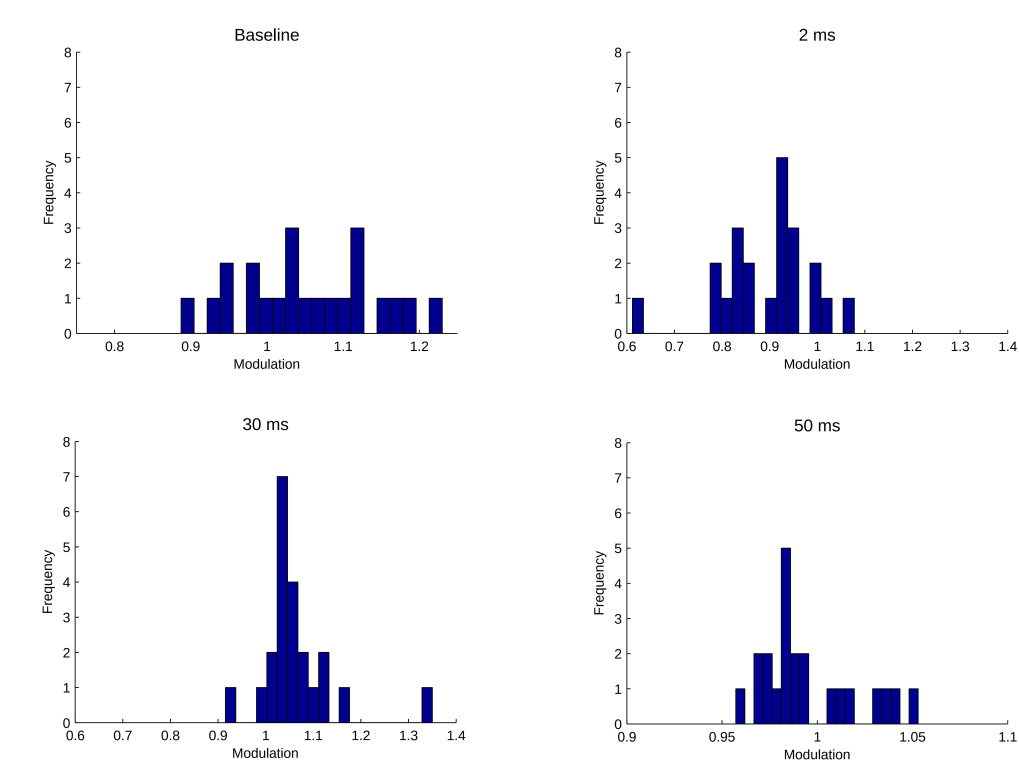
Simulated Data

STN Data



- In simulation, the estimates tend to follow the true parameter values closely
- In the data, the separation between the 95% confidence regions suggests a significant change in rhythmic spiking dynamics
- In simulation, the test detects as little as 2.4% modulation in these parameters with high power
- In the data, the majority of cells show significant changes in rhythmic spiking dynamics

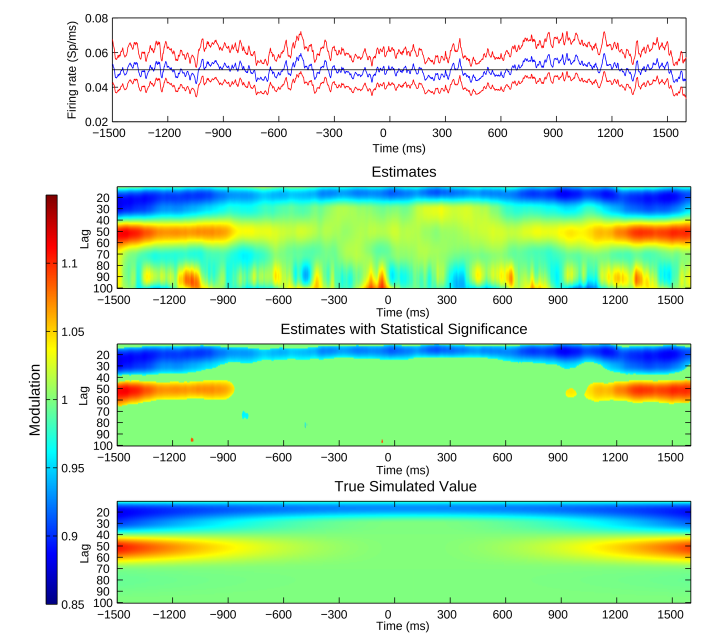
STN Data



- We observe a release in inhibition 30 ms after a spike across nearly all cells and a decrease in excitation 50 ms after a spike for a majority of cells
- Suggests that a complex pattern of neural firing is modulated consistently by movement

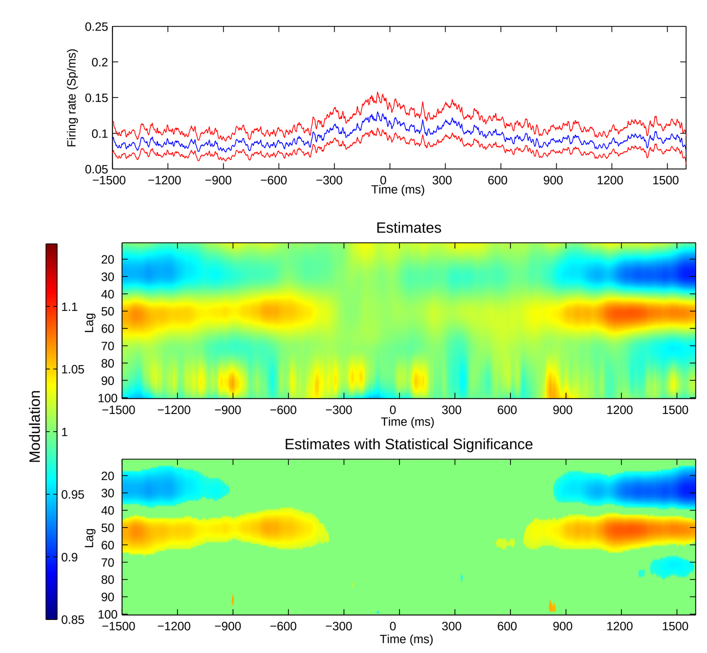
Tracking Changes in Spiking Dynamics

Simulated Data



- 95% confidence bounds about the baseline rate correctly contain the true value at all times
- The estimated trajectories of the modulation parameter values follow the true simulated values closely at all lags and times
- Large regions with considerable modulation in history dependence are identified as significant, while transient changes in modulation are not
- Dynamics can be tracked with a high degree of confidence

STN Data



- We identify an increase in the baseline firing intensity as a function of movement, and characterize its time course
- We track changes in inhibitory modulation parameters around 30 ms and in excitatory modulation parameters around 50 ms as a function of movement
- Suggests a dynamic pattern of transition between spiking states, whereby the change in rhythmic spiking at beta frequencies initially comes about by a reduction in inhibitory control of spiking, which is followed by reduction in excitatory control at the beta period and a simultaneous increase in baseline firing rate

Important Features of the Proposed Framework

- Need not assume a stationary spiking process.
- Provides a great deal of flexibility in assessing relationships between the instantaneous probability of spiking, the past spiking history, and other covariates.
- Allows us to examine the effects of multiple model components simultaneously.
- Provides a powerful hypothesis test for identifying subtle changes in the firing dynamics.
- The state space approach can characterize critical transitions in rhythmic spiking dynamics.
- Maintains adaptive estimates of mean and covariance structure, permitting the construction of confidence intervals and the identification of interactions between covariates.

References

- R. Amirnovin, Z. M. Williams, G. R. Cosgrove, and E. N. Eskandar, "Visually guided movements suppress subthalamic oscillations in Parkinson's disease patients," J. Neurosci. **24**, 11302 (2004)
- U. T. Eden, L. M. Frank, R. Barbieri, V. Solo, and E. N. Brown, "Dynamic analysis of neural encoding by point process adaptive filtering," Neural Comput. **16**, 971 (2004)
- U. T. Eden, J. T. Gale, R. Amirnovin, and E. N. Eskandar, "Characterizing the spiking dynamics of subthalamic nucleus neurons in Parkinson's disease using generalized linear models," Front. Integr. Neurosci. **6**, 28 (2012)
- W. Truccolo, U. T. Eden, M. R. Fellows, J. P. Donoghue, E. N. Brown, "A point process framework for relating neural spiking activity to spiking history, neural ensemble, and extrinsic covariate effects," J. Neurophysiol. **93**, 1074 (2005)