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# Adaptive Prediction of High-Voltage Spindles for Closed-loop DBS Applications in Parkinson's Disease

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## Abstract

Parkinson's disease (PD) is a severely disabling neurodegenerative movement disorder with insidious pathogenesis in the cortico-basal ganglia networks. The open-loop deep brain stimulation (DBS) is a conventional treatment for advanced PD patients by continuous electrical stimulation to the target nuclei. Due to their non-adaptive characteristics, side-effects and limited efficacy in PD patients, there has been a pressing need for the adaptive closed-loop DBS systems. The waxing-and-waning high-voltage spindles (HVSs) have been observed in the local field potentials (LFPs) recorded from the basal ganglia network of PD rat models. The synchronous spike-and-wave HVSs are related to the immobile behavior in PD by increased power in theta band (5-13 Hz). The objective of this study is to develop a simple adaptive algorithm to deliver the stimulation current only at the occurrence of HVSs to realize a demand-driven closed-loop DBS system. A low-order time-varying autoregressive (TVAR) model is derived from the temporal properties of HVS oscillations. For every short segment of real LFPs, the adaptive Kalman filter trains the model parameters (1) to give reliable instantaneous spectral estimates for the early-onset detection of HVSs, and (2) to predict the characteristic dynamics of HVSs. The prediction performance of the algorithm is validated with the LFPs recorded from eight brain regions of different PD rats. The low model order and simple architecture facilitate the hardware implementation of LFP-driven closed-loop DBS for suppressing HVSs in real time. Therefore, the proposed algorithm would underpin the development of a closed-loop neuromodulator for treating PD or other neurodegenerative disorders.

## Materials and Methods

The PD rat models were induced in 3-4 months old Sprague-Dawley rats by unilateral injection of 6-hyrdoxydopamine (6-OHDA) in the medial forebrain bundle at the rate of 0.5 µl/min. The LFPs are recorded from eight brain regions including layers 5b and 2/3 of the primary motor cortex, layers 5b and 2/3 of the secondary motor cortex, layers 5b and 2/3 of the primary somatosensory cortex, the dorsal region of striatum, and the ventrolateral thalamus.

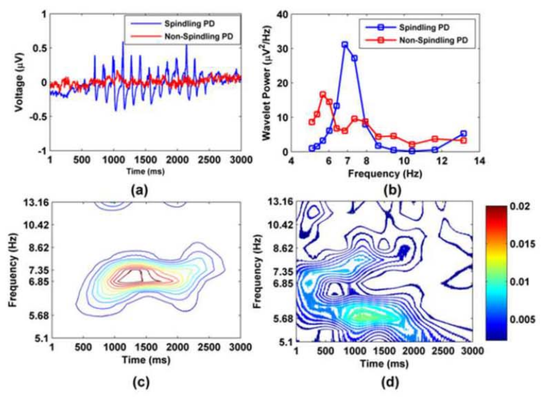


Figure 1. (a) Time domain representation of raw single-channel spindling and non-spindling LFP segments; (b) Power spectral distributions of the two signals in the frequency band of 5-13 Hz; Time-frequency distributions of (c) Spindling and (d) Non-spindling LFPs.

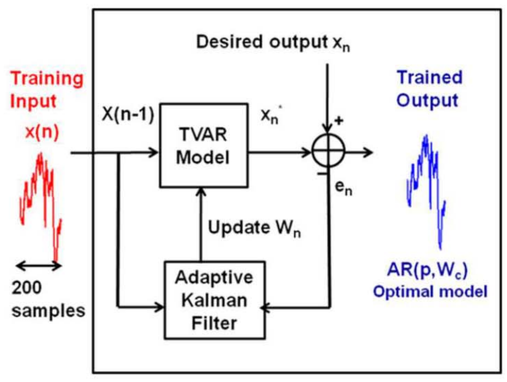


Figure 2. The architecture for realizing the online training phase. The adaptive Kalman filter updates the TVAR model coefficients recursively for every input segment of 200 samples.

## Results

The prediction performance of the algorithm is shown for the sample spindling and non-spindling segments of the real LFP (Fig. 3f) recorded from the layer 5b of the primary motor cortex in PD rat. The TVAR model coefficient vector (W) obtained at the end of training gives the estimated power spectral density (PSD). Fig. 3b confirms the early-onset detection of HVS by the elevated PSD in the theta band. The model also predicts the dynamics of LFPs from 801-1300 ms using the value of W at 800 ms and the LFP segment from 657-800 ms. The occurrence of HVS is further verified by the predicted LFP in Fig. 3c and its time-frequency distribution (Fig. 3e) showing the characteristic symmetrical higher-energy distribution. The algorithm is also successful in responding to the transition from spindling to non-spindling segment at 4200 ms. The estimated PSD in Fig. 4b is very low than that of Fig. 3b. The time-frequency distribution (Fig. 4e) of the predicted LFP (Fig. 4c) exhibits the asymmetric distribution of lower-energy levels.

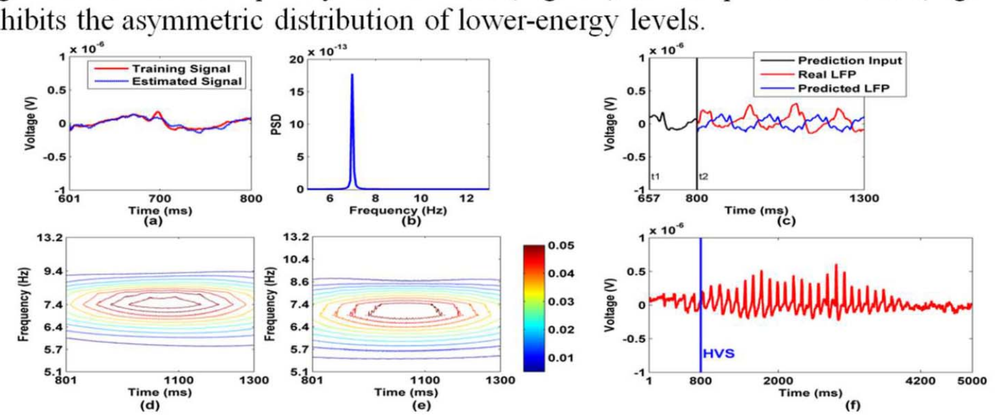


Figure 3. Prediction performance against spindling LFP segment. (a) Training results; (b) Estimated PSD at 800 ms; Time-frequency distributions of (c) Real LFP, and (d) Predicted LFP; (e) Early-onset detection of HVS at 800 ms.

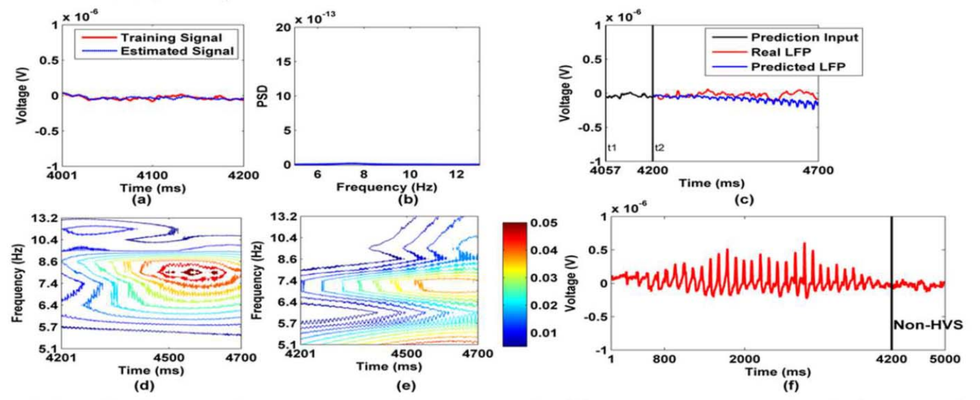


Figure 4. Prediction performance against non-spindling segment. (a) Training results; (b) Estimated PSD at 4200 ms; Time-frequency distributions of (c) Real LFP, and (d) Predicted LFP; (e) Detection of Non-HVS at 4200 ms.

## Conclusion

The HVS prediction algorithm is tested against the LFPs from different brain regions of PD rats to give 90% sensitivity, 88% specificity and 88% accuracy. Hence, this algorithm is suitable for closed-loop DBS applications in the treatment of PD. I am currently working to implement the proposed algorithm in a microcontroller for real-time applications.

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