Journal of Neuroscience Methods 188 (2010) 97–104

Contents lists available at ScienceDirect

Journal of Neuroscience Methods

journal homepage: www.elsevier.com/locate/jneumeth

Detecting and tracking tremor in spike trains using the rectangular model based extended Kalman smoother

Sunghan Kim*, James McNames[1]

Biomedical Signal Processing Laboratory, Electrical & Computer Engineering, Portland State University, Portland, OR, USA

ARTICLE INFO

Article history:
Received 25 November 2008
Received in revised form 21 January 2010
Accepted 21 January 2010

Keywords:
Essential tremor (ET)
Extended Kalman smoother (EKS)
Inter-spike interval
Microelectrode recordings (MER)
Renewal process
Spike train

ABSTRACT

Tremor is one of the most disabling symptoms in patients with movement disorders such as Parkinson's disease (PD) and essential tremor (ET). Spike trains extracted from microelectrode recordings are used to study the relationship of tremor exhibited by neuronal signals to physical tremor as measured with electromyograms (EMG), gyroscopes, or accelerometers. We describe a new method for continuously tracking the instantaneous tremor frequency and amplitude in spike trains based on a new state-space model and the extended Kalman smoother. This method can be used to detect periods of statistically significant tremor in recordings with intermittent tremor.

1. Introduction

Tremor activity can be measured with many types of instrumentation and sensors including electroencephalograms (EEG), magnetoencephalograms (MEG), electromyograms (EMG), accelerometers, gyroscopes, and microelectrode recordings (MER). Most tremor signals are quasi-periodic and nearly sinusoidal.

A number of recent studies have focused on characterizing the relationship of two or more tremor signals. In many cases these signals are obtained from different types of instrumentation (e.g., MER and EMG). One of the surprising findings of these studies is that even when two signals contain significant tremor at the same frequency, these signals are not always coherent or phase coupled (Hurtado et al., 2005, 2000). This suggests that tremor either originates from multiple sources or that the tremor is modulated by uncoupled sources of unknown origin. A few studies have also found that the phase coupling between pairs of tremor signals varies over time (Hurtado et al., 2005, 2004, 1999; Hellwig et al., 2003).

One of the difficulties with studying phase coupling is that this signal behavior cannot be characterized with traditional signal processing and time series analysis techniques that assume that the signals are generated by a linear stochastic process. These methods are essentially blind to subtle nonlinear effects, such as intermittent phase coupling. This presents an opportunity for new signal processing methods that can estimate how the degree of phase coupling between pairs of tremor signals varies over time.

The main goal of the phase coupling study is to measure the degree of synchronization between tremorous activities in two signals. In the phase coupling study, measuring the strength of tremorous activities in each signal is the first task to perform since the phase coupling is meaningful only when tremor is present in both signals. Based on the tremor strength measurement, the signals are segmented into *tremor-on* and *tremor-off* periods. This step is called *tremor detection*. The following step is to track the instantaneous tremor frequency (ITF) of the tremor-on periods. It is common to perform the detection and tracking steps separately.

Hurtado *et al.* conducted the most thorough study of intermittent coupling of tremor signals to date (Hurtado et al., 2005, 2004). They studied the synchronization between tremor-related activities in single unit spike trains and EMG, where spike trains were recorded from globus pallidus internus (GPi) and EMG from the abductor pollicis (APB) in Parkinsonian subjects. Prior to the synchronization study, they first *detected* tremor-on periods of the signals relying on the traditional time–frequency analysis. Their tremor detection algorithm involves setting a threshold for tremor amplitude. They selected a threshold value based on visual inspection of the signal's spectral components. Then, they applied a ITF tracking method based on the Hilbert transform to tremor-on periods of the signals. The Hilbert transform produces an estimate of Gabor's analytic signal. However, spike trains rarely meet the con-

* Corresponding author at: Fourth Avenue Building (FAB), Room 89-02, 1900 SW 4th Avenue, Portland, OR 97201, USA. Tel.: +1 503 725 5390; fax: +1 503 725 3807.
E-mail addresses: sunghan@pdx.edu (S. Kim), mcnames@pdx.edu (J. McNames).
[1] Current address: Fourth Avenue Building (FAB), Room 160-12, 1900 SW 4th Avenue, Portland, OR 97201, USA. Tel.: +1 503 725 5399; fax: +1 503 725 3807.

0165-0270/$ – see front matter © 2010 Elsevier B.V. All rights reserved.
doi:10.1016/j.jneumeth.2010.01.025

ditions necessary for this estimate to be accurate (Boashash, 1992). In particular, the representation of spikes as impulses results in a broad signal bandwidth that makes it difficult to track a single frequency. In Kim and McNames (2006) we demonstrated that the Hilbert transform based ITF tracker does not produce an accurate estimate of ITF.

We propose a method based on the Kalman filter to track the instantaneous tremor frequency (ITF) and amplitude (ITA) simultaneously. Although the Kalman filter is not widely used for frequency tracking, it is a suitable approach for this problem because it is based on an explicit statistical model of the signal that permits the user to incorporate domain knowledge elegantly into the estimator. For example, in this application the observation noise in the spike trains, the amplitude and rate at which the tremor frequency fluctuates, and the typical range of tremor frequencies is either known or can be estimated (Deuschl and Elble, 2000). Since the ITF has a nonlinear relationship with the signal, we applied the extended Kalman smoother (EKS), which uses a first-order Taylor series approximation around estimates of the current state.

Our previous work has demonstrated that the EKF and EKS are suitable methods to track the ITF in spike trains (Kim and McNames, 2006). In this paper we describe an improved state-space model that can track the ITA as well as the ITF. This is a significant improvement over our prior work which assumed a constant tremor amplitude. The state-space model and estimator that we use are similar to those used in Parker and Anderson (1990), but the application is different and we incorporate additional domain knowledge about the process in our model to improve robustness and reduce sensitivity to user-specified parameters.

Rivlin-Etzion et al. (2006) proposed a local shuffling method to overcome the low frequency range spectral distortion of spike trains due to a refractory time. However, in our applications, the spectral distortion was not noticeable since the refractory time was small in comparison to the mean firing rate.

The objectives of this work were to design a tremor tracker that estimates the ITF and ITA of tremorous activities in neuronal recordings continuously and to study the performance of the tracker based on synthetic and real neuronal recordings. The neuronal recordings are widely modeled as point processes consisting of a series of action potentials, or spikes, that are treated as all-or-none events. Most researchers assume that all of the useful information is conveyed in the timing of these events. It is common practice to detect spikes during the early stages of analysis and focus all subsequent analysis on spike trains that consist of a 1 at the time of each spike occurrence and 0 elsewhere. Tremor is exhibited in this signal through pulse frequency modulation that causes fluctuations in the mean firing rate (McNames, 2005). All spike trains in this study are single unit spike trains.

2. Methodology

2.1. Introduction and notation

The Kalman filter recursively estimates the state of a linear stochastic process such that the mean squared error is minimized (Kalman, 1960). Each estimate of the current state is computed based on the previous state and the current observation. The Kalman smoother is a non-causal estimator that uses the entire record to estimate the state of a linear stochastic process.

Our statistical model is nonlinear because the ITF is related to the spike train via sinusoids. Therefore, the Kalman filter and smoother cannot be applied directly to it. One way to handle the nonlinearity of the model is to approximate a nonlinear state-space model by a local linear approximation of the model. The extended versions of the Kalman filter (EKF) and smoother (EKS) recursively estimate the state of a nonlinear stochastic process relying on the local linear approximation of the nonlinear state-space model. Since the state estimates are calculated recursively, the computational requirements are quite manageable for most applications.

We used boldface notation to denote random processes, normal face for deterministic parameters, upper case letters for matrices, lower case letters for vectors and scalars, and subscripts for time indices. The spike train or simply spike train is denoted as $\boldsymbol{y}_n$ where $n = 0, \ldots, N$ is the independent variable representing discrete time.

2.2. Rectangular observation model

We use the following observation model

$$\boldsymbol{y}_n = \boldsymbol{a}_n \cos\left(\boldsymbol{\theta}_n\right) + \boldsymbol{b}_n \sin\left(\boldsymbol{\theta}_n\right) + \bar{\boldsymbol{y}}_n + \boldsymbol{v}_n \quad (1)$$

where $\boldsymbol{a}_n$ and $\boldsymbol{b}_n$ are the amplitudes of two sinusoidal components, $\bar{\boldsymbol{y}}_n$ is the trend, and $\boldsymbol{v}_n$ is a white noise process with zero-mean and variance r. We define the instantaneous tremor amplitude (ITA) as

$$\boldsymbol{c}_n \triangleq \sqrt{\boldsymbol{a}_n^2 + \boldsymbol{b}_n^2} \quad (2)$$

In the terminology of Parker and Anderson (1990), this is called a rectangular model. Other mathematically equivalent models have been used for frequency tracking with the extended Kalman filter (Parker and Anderson, 1990; La Scala et al., 1995, 1996; Bittanti and Savaresi, 2000; Kim and McNames, 2006), but the performance of these trackers varies due to differences in the linearization errors. We have chosen the rectangular model because it is linear in the state variables $\boldsymbol{a}_n$, $\boldsymbol{b}_n$, and $\bar{\boldsymbol{y}}_n$ and should therefore introduce less error in the linear approximations that the EKF relies on.

In most Kalman filter applications the measurement noise $\boldsymbol{v}_n$ is assumed to be white and Gaussian. However, the Kalman filter recursions are still optimal in that they minimize the mean square error (MSE) even if the noise does not have a Gaussian distribution, so long as it is white. A Poisson point process is another example of a random process that is white, even though the distribution of the point process is binary-valued and non-Gaussian. A spike train with tremor contains a systematic fluctuation in the firing rate and is not a white noise process, but the systematic fluctuation can be modeled as a slowly varying trend and a sinusoidal component. The remaining fluctuations in the spike train are reasonably modeled as a white noise process, which permits us to use the observation model in (1).

2.3. Process model

The state of this process consists of the instantaneous phase $\boldsymbol{\theta}_n$, instantaneous frequency $\boldsymbol{f}_n$, trend $\boldsymbol{y}_n$, and the coefficients $\boldsymbol{a}_n$ and $\boldsymbol{b}_n$. We model fluctuations in the instantaneous phase as a first-order approximation of an integral of the instantaneous frequency,

$$\boldsymbol{\theta}_{n+1} = \mathrm{mod}_{2\pi}\{\boldsymbol{\theta}_n + 2\pi T_s s\left[\boldsymbol{f}_n\right]\}, \quad (3)$$

where $T_s = 1/f_s$ is the sampling interval. The modulus operator, $\mathrm{mod}_{2\pi}$, has no effect on the model mathematically, but keeps $\boldsymbol{\theta}_{n+1}$ bounded to $0 \le \boldsymbol{\theta}_n \le 2\pi$ and reduces roundoff error.

The instantaneous tremor frequency (ITF) of the process is defined as

$$\boldsymbol{f}_{i,n} = s\left[\boldsymbol{f}_n\right], \quad (4)$$

where $s[\cdot]$ is a squashing function or limiter that prevents the ITF from exceeding user-specified limits, $f_{\min} \le \boldsymbol{f}_{i,n} \le f_{\max}$. Throughout