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Comparison of methods for estimating motor unit firing rate time series from firing times

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ABSTRACT

The central nervous system regulates recruitment and firing of motor units to modulate muscle tension. Estimation of the firing rate time series is typically performed by decomposing the electromyogram (EMG) into its constituent firing times, then lowpass filtering a constituent train of impulses. Little research has examined the performance of different estimation methods, particularly in the inevitable presence of decomposition errors. The study of electrocardiogram (ECG) and electroneurogram (ENG) firing rate time series presents a similar problem, and has applied novel simulation models and firing rate estimators. Herein, we adapted an ENG/ECG simulation model to generate realistic EMG firing times derived from known rates, and assessed various firing rate time series estimation methods. ENG/ECG-inspired rate estimation worked exceptionally well when EMG decomposition errors were absent, but degraded unacceptably with decomposition error rates of $\geqslant 1\%$. Typical EMG decomposition error rates—even after expert manual review—are 3–5%. At realistic decomposition error rates, more traditional EMG smoothing approaches performed best, when optimal smoothing window durations were selected. This optimal window was often longer than the 400 ms duration that is commonly used in the literature. The optimal duration decreased as the modulation frequency of firing rate increased, average firing rate increased and decomposition errors decreased. Examples of these rate estimation methods on physiologic data are also provided, demonstrating their influence on measures computed from the firing rate estimate.

1. Introduction

The central nervous system regulates recruitment and firing rates of motor units (MUs) to modulate overall muscle tension (Henneman et al., 1965; Milner-Brown et al., 1972, 1973a, 1973b). For active MUs, firing rate—and other measures derived from it—have been studied during healthy physiologic states, including: constant-force contractions (DeLuca et al., 1996), slowly increasing force contractions (DeLuca et al., 1982a,b; Milner-Brown et al., 1973b), fatigue (Bigland-Ritchie et al., 1983), muscle pain (Farina et al., 2004), physical training (Duchateau et al., 2006) and aging (Kallio et al., 2012; Christie and Kamen, 2009); and during disease states (Dietz et al., 1974; Dorfman et al., 1989; Gemperline et al., 1995; Kasi et al., 2009; Rice et al., 1992). This research remains ongoing.

By "firing rate," we are referring to the firing rate *time series*. To study firing rate, indwelling electrodes are typically used to record the electromyogram (EMG). This EMG is decomposed into its constituent MU firing times, from which individual MU firing rate information is extracted. Recently, surface arrays have also been used to identify MU firing times (Holobar and Zazula, 2004, 2007). In either case, the firing times are generally modeled as a stochastic point process, formed as a result of the underlying time-varying firing rate. Typically, simple information extraction techniques were used to estimate statistical *parameters* of the EMG firing rate time series. Kamen et al. (1995) estimated average firing rate during maximum-effort contractions from the five shortest inter-discharge intervals (IDIs) during a steady-state portion of contraction, excluding doublets (IDI < 10 ms) and long IDIs (>200 ms). Gerdle et al. (2008) used the median firing rate of constant-force contractions to produce an estimate that was less sensitive to possible missed MU action potential (MUAP) detections. Navallas et al. (2014, 2015) used maximum likelihood estimation to improve computation of the IDI mean and standard deviation during constant-force contractions. Some researchers

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have developed estimators of the complete (time-varying) firing rate time series, to facilitate more advanced characterization of its evolution, e.g. the "onion skin" effect, inter-unit synchronization and common drive (DeLuca et al., 1982a; DeLuca, 1985; Stashuk and DeLuca, 1989). Lepora et al. (2009) estimated firing rate from the number of firings in contiguous 50 ms time intervals, pooling data across ensemble trials to assure a sufficient number of firings per interval. Stashuk (2001) estimated firing rate at each firing time as the inverse of a Hamming weighted average of 10 IDIs centered about the firing time, excluding outlier intervals. DeLuca et al. (1982a) estimated firing rate by convolving an impulse train corresponding to the MU firing times with a non-causal (zero phase) 400 ms duration Hanning filter. Physiologically, multiple central nervous system factors contribute to motor nerve excitation and the resulting MU firing times. However, these various factors cannot be directly recorded. Thus, the absence of a physiological "gold standard" makes it difficult to objectively assess the accuracy of firing rate time series (and parameter) estimates. We are not aware of rigorous assessment of firing rate time series estimation methods within the EMG field.

More sophisticated models and methods of firing rate time series analysis have been applied to studies of the nervous system and heart rate (Bayly, 1968; Berger et al., 1986; Mateo and Laguna, 2000). In particular, the continuous-time integral pulse frequency modulation (IPFP) model, adapted for implementation in discrete time, has been used to simulate firing times from a firing rate time series. These firing times can be supplied to a firing rate time series estimation algorithm, and then the estimated rate compared against the "true" rate at each discrete time. Within the ECG literature, robust performance comparisons have been made between advanced firing rate estimators using this model: Berger et al. (1986) estimated heart rate by analytically convolving the continuous-time instantaneous heart rate with a rectangular window function and then analytically sampling the result, while Mateo and Laguna (2000) used spline functions to smooth the instantaneous heart rate (directly in discrete time). In each case, the instantaneous rate was defined as the inverse of the IDI throughout the duration of each IDI.

In this study, we used the IPFM model to simulate MUAP firing times from various firing rate profiles and then quantitatively evaluated several firing rate time series estimators drawn from both the EMG and ECG literature. Our goal was to rigorously cross-compare these estimators. Of particular interest was the performance of each rate estimator in the presence of firing detection/classification errors. In the ECG field, detection errors have been reported as quite low (particularly during recording at rest), certainly under 0.7% (Pan and Tompkins, 1985). In contrast, detection errors in EMG decomposition have been reported as much higher; errors of 3–5% were reported even when automated decomposition is augmented by exhaustive manual editing (Erim and Lin, 2008), and considerably higher (10–20% or more) with automated decomposition or with low-amplitude MUAP trains (Nawab et al., 2008). Hence, our simulations compared performance across a range of false positive and missed detection rates. Lastly, examples drawn from physiologic recordings were used to illustrate the performance of the different firing rate estimation algorithms.

2. Methods

2.1. Integral Pulse Frequency Modulation (IPFM) model and firing rate estimators

All processing was performed in discrete time, but portions are based on initial continuous-time steps. Firing times in our simulations were generated as the output of the IPFM model, given a firing rate as input. In a continuous-time IPFM model, every two consecutive firing times t_k and t_{k+1} were related as (Bayly, 1968):

$$1 \text{ pulse} = \int_{t=t_k}^{t=t_{k+1}} [f_o + f_{Mod}(t)]dt \tag{1}$$

where $f_o > 0$ was the average firing rate in pulses/s (pps) and $f_{Mod}(t) \geqslant -f_0$ was the zero-mean rate modulation as a function of time, t, in pps. Thus, the instantaneous firing rate equaled: $f_o + f_{Mod}(t)$, where this sum was non-negative. Essentially, the integral summed the instantaneous rate until a threshold of 1 pulse was achieved, a simulated firing then occurred at that time and the integral was reset for accumulation during the next IDI. For a constant firing rate, $f_{Mod}(t) = 0$. We implemented this model in discrete time using a discrete sum with a sampling interval of 1/40,960 s. Firing times were rounded to the nearest 1/4096 s, to correspond to the sampling rate of the firing rate estimators. For one simulation, this model produced a set of N time-increasing firing times $\vec{t}_F = \{t_1, t_2, t_3, \ldots t_N\}$.

Firing rate estimators (in pps) were compared using a sampling rate of F_s = 4096 Hz. Rate estimation was made from each firing time vector $\vec{t}_F$. The *continuous-time* "instantaneous" rate, $r_{Inst}(t)$, was defined at time t (t being located between firing times t_k and t_{k+1}) as the inverse of the IDI in which t was located:

$$r_{Inst}(t) = \frac{1}{t_{k+1} - t_k}. \tag{2}$$

Short duration IDIs corresponded to large firing rates; long duration IDIs corresponded to small firing rates. The rate was constant between firing times and changed in a step fashion at the next firing time. The *discrete-time* instantaneous rate used in our analysis, $r_{Inst}[n]$ (where n was the sample index), was computed by periodically sampling $r_{Inst}(t)$. This estimator had no parameters. Since $r_{Inst}[n]$ was a sampled version of the continuous-time instantaneous rate $r_{Inst}(t)$, it suffered from aliasing at the step transitions occurring at each firing time (Berger et al., 1986).

To alleviate this aliasing, Berger et al. (1986) showed that the continuous-time instantaneous rate shown in Eq. (2) can be analytically convolved with a rectangular gate function and then analytically sampled, producing the "Berger" rate, $r_{Berger}[n]$. Convolution in continuous time with a gate function was a form of lowpass filtering that limits the aliasing. The Berger rate calculation can be thought of as:

$$r_{Berger}[n] = \left\{ r_{Inst}(t) \otimes \mathrm{Rect}_{T_B}(t) \right\}\Big|_{t=\frac{n}{F_s}}, \tag{3}$$

where $\mathrm{Rect}_{T_B}(t) = \left\{ \begin{array}{ll} \frac{1}{T_B}, & \frac{-T_B}{2} < t < \frac{T_B}{2} \\ 0, & \text{otherwise} \end{array} \right\}$. Parameter T_B was varied between 40 and 1600 ms in increments of 40 ms. Note that the lowpass analytic convolution distorted the spectrum of the firing rate. Berger et al. corrected for this distortion—but with a technique that was only useful at low frequencies. We did not apply their correction.

The "DeLuca" rate (DeLuca et al., 1982a) was formed directly in discrete-time. Time-series $\delta_F[n]$ equaled one at the sample location closest to each firing time, and zero otherwise. Then,

$$r_{DeLuca}[n] = \delta_F[n] \otimes \mathrm{Hann}_{T_D}[n], \tag{4}$$

where $\mathrm{Hann}_{T_D}[n]$ was a non-causal (zero-phase) Hanning window. The window duration T_D was varied between 40 and 1600 ms in increments of 40 ms.

Mateo and Laguna (2000) created a smoothed firing rate by initially assembling the previously defined N-length vector of (non-periodic) firing times, $\vec{t}_F$, as the x-axis vector; and the staircase vector $\{1, 2, 3, \ldots N\}$ as the y-axis vector. The y-axis values