Efficient peripheral nerve firing characterisation through massive feature extraction

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Abstract—Peripheral nerve decoding algorithms form an important component of closed-loop bioelectronic medicines devices. For any decoding method, meaningful properties need to be extracted from the peripheral nerve signal as the first step. Simple measures such as signal amplitude and features of the Fourier power spectrum are most typically used, leaving open whether important information is encoded in more subtle properties of the dynamics. We here propose a feature-based analysis method that identifies changes in firing characteristics across recording sections by unsupervised dimensionality reduction in a high-dimensional feature-space and selects single efficiently implementable estimators for each characteristic to be used as the basis for a better decoding in future bioelectronic medicines devices.

I. INTRODUCTION

Bioelectronic medicines [1] modulate the activity patterns on peripheral nerves by implanted devices. They form a new way of treatment with promise for many conditions such as hypertension and tachycardia [2], [3], sleep apnea [4], rheumatoid arthritis [5] and many more. Today’s devices are still very simple, however, and mostly operate in an open-loop fashion that is not aware of the current activity on the nerve. For future bioelectronic medicines, closed-loop systems that diagnose the signals on target nerves and only block or stimulate when necessary could be much more efficient and effective. It is thus vital for the progress of the field to investigate ways of continuously or periodically characterising peripheral nerve activity and associating its patterns with the physiological state (‘decoding’) to modulate adaptively.

A first step of such a decoding will be the extraction of meaningful properties from the peripheral nerve recording to then associate with the physiological parameters we seek to estimate. Peripheral nerve recordings possess a low signal-to-noise ratio, due to the weak (~10mV) potentials caused by the axons and other sources of electricity such as muscles. Spatial recording resolution of current non-invasive interfaces (cuff electrodes) is limited as well, making it impossible to differentiate single fibers. The recording is thus made up by compound action potentials (CAP): the superposed activity of many axons in a nerve-bundle. Given these constraints on data quality, decoding is most often based on the amplitude of the rectified and integrated signal [6], [7] or the power (as square of amplitudes from a Fourier spectrum) in a certain frequency band [8].

But are those simple summary values (amplitude, power) sufficient to capture the entire information contained in peripheral nerve recordings or are better measurements possible? Many subtleties are known to exist in peripheral firing such as active fibre diameters, active fascicles and different rhythms [9], many of which will be informative for decoding. If we could identify some of those firing characteristics in a peripheral nerve recording and estimate them in each new observation, we might have a better starting point for decoding. But how can we decide which are the main varying firing characteristics and how can we estimate them—keeping in mind that this estimation has to be very energy-efficient to not deplete the small battery of the implanted device?

One possibility of characterising time series by their dynamical properties is a set of global time series features, of which many have been developed in different disciplines over the past decades [10]. Representing a time series by its dynamical properties using features proved useful for e.g., classification [11], clustering, and forecasting [12]. In this work we seek to leverage the vast literature on time-series features to find better representations of peripheral nerve firing.

Building on a diverse set of over 7 500 time series features [13], [14], we propose an unsupervised analysis method that fulfills two purposes. It (1) automatically infers the types of properties across which peripheral nerve recordings vary most and (2) proposes estimators that quantify these properties (‘characteristics’) in new data. We demonstrate the utility of our approach on simulated data in which the activity characteristics firing rate, myelination ratio, and burstiness were uncovered successfully. The selected estimators for the main peripheral firing characteristics can be efficiently implemented for on-line summarisation of peripheral nerve recordings and thus as a basis for a more accurate decoding in closed-loop bioelectronic medicines.

II. METHOD

A. Time series features

We want to analyse peripheral nerve recordings by their dynamical properties and therefore first need a set of diverse estimators (features) that quantify time-series characteristics. We obtain such a wide array of estimators from the Highly

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Comparative Time Series Analysis (*hctsa*) toolbox [13], [14]. It lets us compute more than 7 500 global time series features from diverse disciplines that measure e.g., basic statistics of value-distributions, linear correlations, stationarity, entropy and many more. Each feature \( f_i(X) \) summarises a time series \( X = [X_1, X_2, ..., X_k] \) of length \( N \) as a single value, \( f_i : \mathbb{R}^N \rightarrow \mathbb{R} \). Using the ensemble of all \( M \approx 7 500 \) features \( F = \{ f_i : i = 1, ..., M \} \), the *hctsa*-toolbox can transfer our peripheral nerve recordings to feature points in an \( M \)-dimensional feature-space \( F(X) : \mathbb{R}^N \rightarrow \mathbb{R}^M \) for characteristics-based analysis.

**B. Detecting the varying characteristics in feature-space**

We analyse datasets in the high dimensional feature-space generated by the *hctsa*-toolbox to detect the dynamical properties (‘characteristics’) that varied over time. See Fig. 1 for a schematic overview of our approach. Using *hctsa*, the dynamics of each single time series will be summarised as a feature vector which can be represented as a single point in feature-space. To obtain a point cloud to analyse, we transfer multiple recording segments to feature-space between which certain dynamical characteristics are different. If characteristics that vary between segments are estimated by some of the computed features, their variation will drive the spread of the point cloud in feature-space. We can thus detect those varying signal properties as the main directions of variance in feature-space using dimensionality reduction methods such as principal component analysis (PCA) or others [15]. These main dimensions make up a low-dimensional space of ‘main varying characteristics’ to project our data into.

On the datasets in this study, up to 1 500 of our initial 7 500 features had special valued outputs and were removed, on average ~6 800 remained. We then normalised each feature by a robust sigmoid transform [13] and retrieved the main directions of spread through PCA.

**C. Selecting efficiently implementable features**

So far we have uncovered the main varying signal characteristics across our recording segments as the principal components (PC) in feature-space. Each of these components will depend on the computation of thousands of single features. To efficiently project new data onto the PCs, we approximate each of them by a single representative feature selected by maximum Pearson correlation to the component.

In this way we devise our set of efficient estimators for the varying signal characteristics in the dataset at hand.

**D. Datasets**

To be in possession of ground truth and to demonstrate the success of our method, we generated surrogate data in the peripheral nerve simulator PyPNS [16]. Four simulated datasets were obtained from a nerve with a fixed length of 5cm containing 500 active axons. For each of the four datasets, we generated 400 to 1000 snippets of length 400ms across which two to three of the firing characteristics myelination ratio (0 - 2%), firing rate (0.1 - 10 spikes/axon/second), and burstiness (0 - 100% of firing probability imbalance between two alternating intervals) varied uniformly. Our method was then trained to detect these characteristics in the unsupervised manner described above.

**III. RESULTS**

**A. Recovery of characteristics**

We want to uncover, in a purely data-driven way, the characteristics that varied in our simulator. To this end we transferred all 400ms-segments of the simulated peripheral nerve recording into feature-space using our *hctsa*-toolbox and found the principal components of their point cloud. Between recording segments, two to three firing characteristics varied and ideally, each of them would be recovered by a single principle component in feature-space. To demonstrate...
this correspondence between PCs and characteristics in a first example, Fig. 3 plots the time series points for the pair of varying characteristics firing rate and burstiness projected onto the first and second PC. As can be seen, firing rate is cleanly captured by the first component, burstiness corresponds to the second. At lower firing rates (to the right of the plots in Fig. 3), burstiness is less distinguishable along PC2, consistent with visual intuition from Fig. 2A and C (burstiness is harder to distinguish for low firing-rate).

As an overview over all our four datasets, Fig. 4A shows the correlation between firing characteristics and each of the first components for datasets with noise-level −6dB (see Fig. 2 for an example recording). On datasets with two varying characteristics, especially in the pairs (burtness, myelination) and (firing rate, burstiness) each characteristic was perfectly recovered by a single PC. For the pair (myelination, firing rate), firing rate was not cleanly separated from myelination which can be explained by the noise amplitude that partly shadowed action potentials from unmyelinated fibres. At three varying characteristics, recovery became less successful. While burstiness and myelination were reasonably captured by the first and second PC, firing rate could not be cleanly separated from the other two characteristics.

B. Robustness against noise

As a measure of how well the main dimensions obtained in dimensionality reduction captured signal characteristics, we linearly regressed each characteristics \( c \) as set in the simulation against the first main dimensions \( D \) (2 main dimensions for 2 varying characteristics, 3 for 3):

\[
\hat{c} = D\alpha + \epsilon. \tag{1}
\]

The unexplained variance \( 1 - R^2(\hat{c}, c) \) gave an estimation of how well the input characteristics could be retrieved by the output of our method. Until a noise RMS of half the signal RMS (−6dB) the characteristics set in our simulation were recovered well, see Fig. 4B. Myelination ratio was the most robust against noise as expected from the high action potential amplitudes from myelinated fibres, burstiness and firing rate could not be well detected at high noise levels.

C. What types of features are selected?

So far we have shown that unsupervised dimensionality reduction in feature-space is a promising way of extracting low-dimensional directions of variation in the underlying system that works well in the majority of our simulated neural firing datasets. But can we interpret each dimension in terms of the signal properties that are being measured, and are they sensible given what we know is varying in the underlying system? To answer these questions, we rank single features by their Pearson correlation to the principal components – and therefore the varying characteristics in the data.

In general, the highest Pearson correlations between single features and principal components reached at least 0.8 and often 0.98 or better, meaning that we can find appropriate representative single features to represent each principle component. For the characteristic myelination ratio, features selected by our method typically evaluate extreme events, outliers, statistics on residuals in local fits. This makes sense as myelinated axons produce very strong peaks. Features corresponding to firing rate components often compute value distribution properties and autocorrelation measures that detect uncorrelated noise vs. natural signals. Burstiness features measure stationarity and predictability. We therefore automatically identify sensible features.

The selected estimators will be different for every dataset and the purpose of this study is not to select a fixed set of features for real world data from our simulated demonstration datasets. The method has to be rerun for a dataset to analyse as each recording will be different in the composition of fibres, the firing patterns and the interface.

D. Comparison to standard methods

Our method is able to detect the main varying characteristics in a peripheral nerve recording and select single estimators for them. What would the state-of-the-art characterisation of peripheral nerve activity have made of our data? For a brief comparison of our method to the standard power-measure RMS, we added its Spearman rank correlations to the characteristics set in our simulation in Fig. 4A. Naturally, with a univariate power measure, no distinction between different firing characteristics is possible. Interestingly however, our first principal component behaves largely identical with RMS in terms of correlation to the data characteristics. In the following PCs, more subtle dynamical properties such as burstiness and myelination were recovered. The estimators selected by our method thus cover all signal properties captured by state-of-the-art measures but importantly provide additional information about more subtle firing characteristics.

IV. CONCLUSIONS

Peripheral nerve decoding algorithms will play an important role in the development of closed loop bioelectronic medicines devices. To date the analysed recordings
have been characterised by simple amplitude- or power-based measures. We here demonstrate the feasibility of automatically extracting feature-based estimators for the main varying firing characteristics, and provide simpler estimators for each. Our method is successful on simulated peripheral nerve recordings in which two independent peripheral firing characteristics could be recovered cleanly in most cases. The method provides a low dimensional representation of the data in meaningful dynamical properties that is more informative than the state-of-the-art characterisation by simple power measures. The selected single estimators for important dynamical properties of peripheral firing can be implemented efficiently for the use in next generation bioelectronic medicines devices and the method may find application in related BMI applications as well.

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REFERENCES


