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An Enhancement to Velocity Selective Discrimination of Neural Recordings: Extraction of Neuronal Firing Rates

Benjamin Metcalfe, Daniel Chew, Chris Clarke, Nick Donaldson and John Taylor

Abstract — This paper describes improvements to the theory of *velocity selective recording* (VSR) of neural signals. Action potentials are classified and differentiated based on their conduction velocities which can be calculated from concurrent neural recordings taken at different locations on a nerve. Existing work has focussed primarily on electrically evoked *compound action potentials* (CAPs) where only a single evoked response per velocity is recorded. This paper extends the theory of VSR to naturally occurring neural signals recorded from *rat* and attempts to identify the level of activity (firing rates) within particular velocity ranges.

I. INTRODUCTION

The theory of *velocity selective recording* (VSR) has been well documented and relies on the fundamental principle that the conduction velocity of neural traffic *electroneurogram* (ENG) on an axon is directly related to its diameter and hence to its underlying biological function. This relationship was first demonstrated by Erlanger and Gasser in 1937 and has been exploited with some success to detect and diagnose various nervous system disorders [1]. Many existing methods for identifying neural signals (ENG) rely on recording from small bundles of axons [2]. This is a difficult process that often requires stranding the nerve into smaller bundles, a procedure that can be destructive to the nerve [3]. The development of advanced neural prostheses requires the non-destructive extraction of more information from neural signals and the use of velocity discrimination is an attractive approach. Existing work has focussed on measuring conduction velocity using *multiple electrode cuffs* (MECs) [4], [5]. These contain several electrodes mounted at precise intervals and can be implanted chronically by being wrapped or curled around an intact nerve. Velocity profiles can be calculated by measuring the time taken for an *action potential* (AP) to travel along the length of the cuff as a function of the inter-electrode spacing. Such velocity profiles have been measured for electrically-evoked *compound action potentials* (CAPs) in *pigs*, *frogs* and other animals (e.g. [6] & [7]).

This paper presents new methods and results that extend the earlier work using CAPs as described in [6] and [8] to recordings of *naturally evoked* ENG. In order to record natural (physiological) ENG successfully it is crucial to be

able to record the arrival time of each AP in addition to its propagation velocity since sensory information is encoded in the firing rates of neurons [9]. New methods are described that permit the calculation of both the velocity spectrum and the neural firing rates as a function of velocity, the *velocity spectral density* (VSD). In order to validate the new methods, acute *in vivo* recordings were made from the L5 dorsal root of a *rat* using an array of 6 *hook* electrodes. Whilst as already noted, cuff-based systems are preferred for chronic implantation, the use of hooks enables individual ENG spikes to be observed and counted which is crucial in the validation process. The acute *in vivo* experiments are described in a companion paper [13].

II. THEORY

A. Compound Action Potentials

VSR is well suited to the analysis of single event APs such as those typically found in electrically evoked CAPs. The stimulation current causes every neuron within the nerve (for which the stimulation current is above the neuron's threshold) to fire. The inherent time synchronisation produces large single responses for each underlying velocity population (Fig. 1). These responses are the direct result of the superposition from many single neurons firing at once.

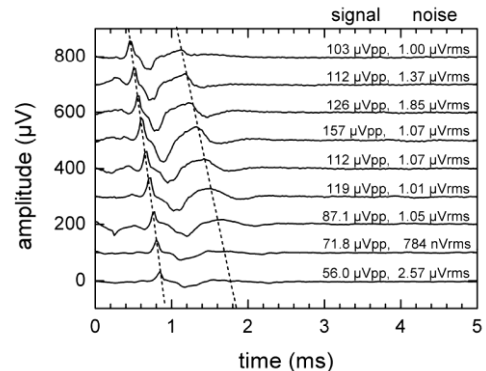


Figure 1: An example of electrically evoked CAPs recorded from nine tripoles in pig median nerve. Electrical stimulus was 4 mA and the dominant velocity populations are 60 m s⁻¹ and 30 m s⁻¹[8].

This is not true for naturally occurring, or physiological, neural signals where individual neurons are firing independently from each other. Information within the nervous system is transmitted in an encoded fashion; the number of APs propagating through a single axon per second is representative of the sensory (analogue) input signal to that axon [9]. This feature is a direct result of the *all-or-nothing* nature of the neuron. As an example, the *afferent*

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fibres that contain information about the fullness of the bladder have been measured in man to propagate at a velocity of 41 m s^{-1} with a baseline firing rate of about 15 APs per 200 ms and a rate representing a full bladder of about 40 APs per 200 ms [10].

The contribution of this paper is the extension of VSR to include information about the number of APs occurring in a given time period. The result is a *velocity spectral density* (VSD) that is a measure of the time varying activity within a band of conduction velocities.

B. Velocity Selective Recording

The basic principle of VSR is to transform time domain recordings of neural signals into the velocity domain. The spectrum of the velocity domain shows both the direction of AP propagation (either *efferent* or *afferent*) as well as the level of excitation of each fibre population within the nerve. A simple process termed *delay-and-add* is commonly used to carry out this transformation [4]. Recordings are made at equal distances along the nerve using a MEC or other linear electrode array. The channels are delayed relative to the first channel V_{B1} by an interval that depends on both the electrode spacing and the propagation velocity of the signal. So if the delay between the first two channels (V_{B1}, V_{B2}) is dt the delay between the first and third channels (V_{B1}, V_{B3}) is $2 \cdot dt$ and so on. Delay-and-add operates by inserting variable delays into the channels to effectively cancel the naturally occurring delays after which the channels are summed resulting in a single signal V_D (1).

$$V_D(t, dt) = \sum_{i=1}^5 V_{Bi}(t(i-1) \cdot dt) \quad (1)$$

The value of dt is swept over a range that corresponds to the velocities within the nerve. For each value of dt the maximal value of V_D is found resulting in a single point within the *intrinsic velocity spectrum* (IVS). This process can be demonstrated using a simulated recording with two single APs with conduction velocities of 10 m s^{-1} & 15 m s^{-1} and with time offsets of 8 ms and 10 ms from the start of the recording respectively. Simulated APs were generated using a *transmembrane action potential* (TMAP) model [4]. There were nine bipolar channels of data sampled at 500 kS/s with an electrode spacing of 1 mm and a cuff length of 9 mm. The IVS (Fig. 2) clearly shows two peaks within the velocity domain. These peaks correspond to the conduction velocity of the APs in the time domain, i.e. 10 m s^{-1} & 15 m s^{-1} . However if another AP is added to the time domain with a conduction velocity matching either existing AP then there is no change in the velocity domain. The maximum value of the time window at any given delay dt has not changed. This is a limitation of the method; there is no information about the number of APs occurring per second.

C. Velocity Spectral Density

The most basic method to extract both conduction velocity and firing rate from a nerve recording is to use a sliding time window of sufficient length to enclose fully a single AP. Existing methods can then be applied to find the IVS of the window contents and hence the most likely peak velocity of the AP.

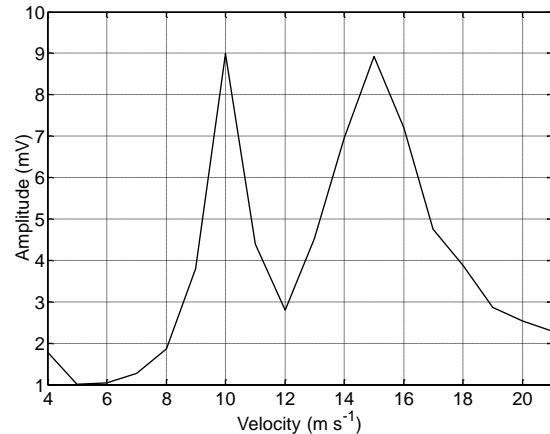


Figure 2: Intrinsic Velocity Spectrum indicating two velocity populations at 10 m s^{-1} & 15 m s^{-1} respectively.

This information can be used to construct a histogram showing the firing rate for each conduction velocity. However this method has two considerable drawbacks: firstly the window must only ever contain a single AP, otherwise only the AP with the largest amplitude will be correctly identified. Secondly the time window used must be carefully selected to avoid *velocity spectral leakage* (VSL), an effect which is similar to its frequency domain namesake and is caused by only a fraction of the AP being visible within the window. A more robust method discards the use of a sliding time window and instead performs automatic detection of APs using the intrinsic relationship between correlated channels based on the complete time record. The method can be broken down into the following steps:

1. The previously described delay-and-add process is applied to the complete time record over the range of conduction velocities of interest (Fig. 3).
2. A single noise threshold is applied that removes any samples below the system noise floor. At present the noise floor for experimental results is computed from the input-referred noise measured in the experiments described in Section III.
3. After delay-and-add, every pulse in V_D is reduced to an impulse by computing the location of its centre of gravity (referred to as its *barycentre*) and applying a simple gate (Fig. 4). The barycentre of a pulse of length n samples is computed using equations (2) and (3) [11]. This computation is performed about the peak of each pulse; n is chosen to be the width of the detection window (i.e. the width of an AP).

$$B_x = \frac{1}{6A} \sum_{i=0}^{n-1} (x_i + x_{i+1})(x_i y_{i+1} - x_{i+1} y_i) \quad (2)$$

$$A = \frac{1}{2} \sum_{i=0}^{n-1} (x_i y_{i+1} - x_{i+1} y_i) \quad (3)$$

Since in practice AP shapes are not regular or symmetric like the simulated examples shown in Fig 3, this method provides a more accurate representation of the location in time of the APs than simply taking the peak values as has been done previously [4], [5]. Finally a detection algorithm is applied that examines each velocity response for the criterion $V_{D-1} < V_D > V_{D+1}$. If this criterion is met the histogram for the current window can be incremented at the velocity V_D . The length of histogram to keep is dependent on the desired time resolution and this is chosen by periodically resetting the histogram values for any velocity. For example the afferents in man corresponding to bladder fullness can occur at up to 40 times per 200 ms in each axon [10], however it is more useful to record bladder fullness over a longer period of time and so the histogram bins would be reset only very infrequently.

III. SIMULATED AND MEASURED RESULTS

In order to illustrate better this process and to validate the methodology, experiments were performed on both simulated data and data recorded *in-vivo* from *rat*. The TMAP model [4] was used to generate a time series 100 ms long, which contained ten APs of arbitrary velocities and time offsets chosen at random. Table I lists the conduction velocities and time offsets for each AP within the time series. The data was generated using a sample rate of 500 kS/s, an electrode spacing of 1 mm and a total of ten bipolar channels representative of a short MEC [12].

The ten bipolar channels were filtered using a bank of delay-and-add processors spaced at 1 m s^{-1} velocity steps over the range 5 to 15 m s^{-1} . The electrode spacing of 1 mm and a sample rate of 500 kS/s requires delays of $200 \mu\text{s}$ to

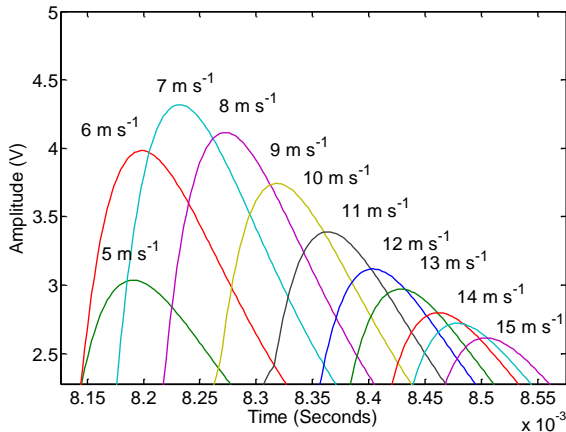


Figure 3: Close-up of the delay-and-add waveforms (V_D) for an action potential of 7 m s^{-1} illustrating the characteristic amplitude maximum at the matched velocity.

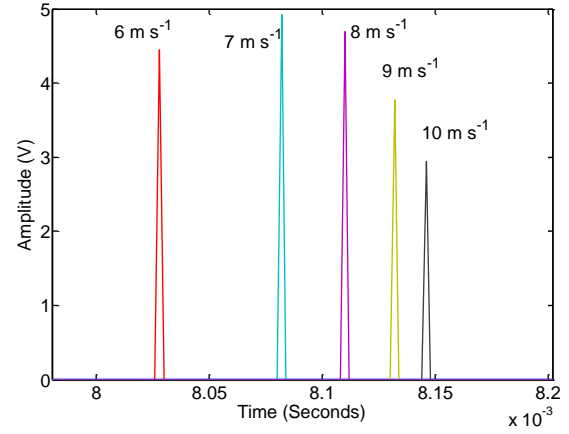


Figure 4: Close-up of the delay-and-add waveforms (V_D) for an action potential of 7 m s^{-1} after gating at the barycentre of each velocity. Noise threshold = 3.5 V .

$66.6 \mu\text{s}$. The VSD was used to generate a histogram representing the firing rates of each velocity over the time window (Fig 5). These automatically computed velocities were compared to the values used to generate the time series (Table II). The automatically detected velocities matched perfectly, the detected time offset for each AP was shifted slightly in time. This is an artefact of the delay-and-add process as the peak response is generated at the centre of the AP as opposed to the start.

Table I:

Conduction velocity and time offsets of the ten artificially generated APs.

ID	Velocity (m s^{-1})	Time Offset (ms)
1	7	8
2	6	16
3	7	22
4	8	50
5	8	55
6	7	62
7	6	70
8	13	76
9	10	84
10	7	90

Table II.

Detected conduction velocity and locations of the ten artificially generated APs.

ID	Velocity (m s^{-1})	Time Offset (ms)
1	7	8.08
2	6	16.09
3	7	22.08
4	8	50.07
5	8	55.07
6	7	62.09
7	6	70.09
8	13	76.05
9	10	84.08
10	7	90.08

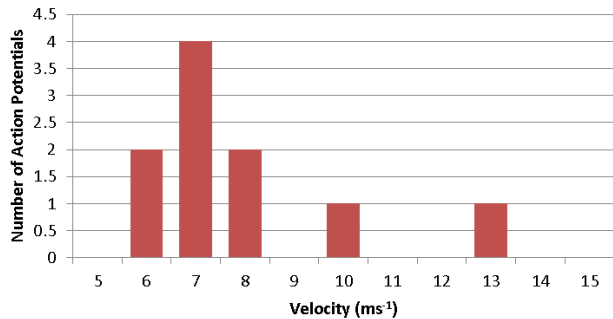


Figure 5: VSD histogram for 100 ms of simulated data containing ten action potentials.

Finally, in order to provide some preliminary validation of the theory presented in this paper, acute *in-vivo* recordings were made from a *rat*. These experiments were part of a larger study that is not included here [13]. The recording setup consisted of five bipolar recordings taken from a set of six hook electrodes placed on a fascicle of the L5 dorsal root. For consistency with the simulated data, the electrode spacing was 1 mm and the sample rate was 500 kS/s. The data was captured and processed using MATLAB R2012b (The MathWorks, Natick, MA, USA) in the same manner as the simulated data reported above. The recordings were of length 250 ms and were made both with and without cutaneous stimulation of the L5 dermatome. In order to identify the effect of cutaneous stimulation of the dermatome, direct electrical stimulation was used to identify the conduction velocities of the relevant afferents. VSD analysis applied to the data showed consistent levels of activity in both sets of natural recordings with a significant increase in the number of APs propagating at 10 m s⁻¹ during cutaneous stimulation (Fig. 6). This was in agreement with direct electrical stimulation of the dermatome where CAPs were observed with a conduction velocity of 10 m s⁻¹.

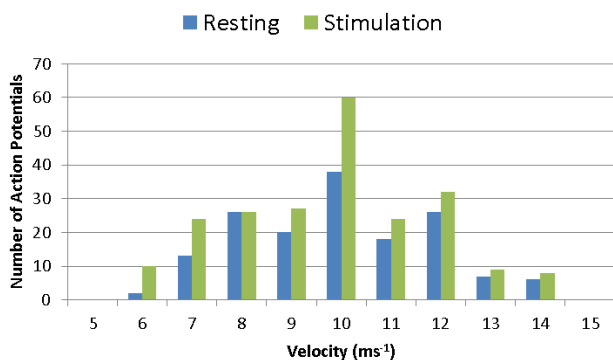


Figure 6: VSD histogram recorded from 250 ms of physiological recordings from *rat* during both resting and cutaneous stimulation.

IV. CONCLUSION

This paper has described a method to extend significantly the capabilities of *velocity selective recording* (VSR) using an automated detection system and a histogram-based analysis of neuron firing rates. This simple method for automatically identifying and classifying APs based on conduction velocity has been demonstrated for simulated data and has been validated by *in-vivo* physiological recordings from the L5 dorsal root in *rat*.

V. ACKNOWLEDGEMENTS

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