Example - Written Assessment: Research Proposal

'The local field potential (LFP): Decodability of motion direction and speed from gamma-band LFPs of neurons in visual area MT of anaesthetised marmosets'

BACKGROUND

A major aim in sensory neuroscience is to understand how the brain represents the external world, and how the electrical activity patterns of neurons lead to the vast range of perceptual experiences available to us. Traditionally, the study of visual perception has focused on the spiking activity within specific regions of the visual system – commonly, the primary visual cortex (V1) and the visual area of the middle temporal region (area MT) (Price & Born, 2013; Kohn & Movshon, 2004; Patterson, Wissig & Kohn, 2013). Area MT is a unique region within the dorsal visual pathway that receives direct inputs from V1 and consists of neurons that selectively represent motion direction and speed (Dubner & Zeki, 1971; Movshon & Newsome, 1996). Furthermore, the responses of neurons in visual area MT are linked with perception - such that the direction and speed of stimulus motion can be determined from changes in single-cell spiking activity (Britten et al., 1992; Salzman et al., 1992). An important caveat of past research, however, is that we know the brain uses the activity of large multi-cellular neuronal populations upon which to make decisions (Quiroga & Panzeria, 2009). Thus, the study of the local field potential (LFP) is becoming more popular as it reflects the integrative synaptic processes of local cell groups that cannot be extracted from spike rates alone (Einevoll et al., 2013).

LFPs contain information regarding the slower (than spikes) electrical oscillations of particular brain regions; with signal powers ranging up to 200 Hz (Crone, Sinai & Korzeniewska, 2006). LFPs may be useful in assessing local neural function at the spatial scale of cortical columns and could shed led light on the computations underlying visual processing in the primate brain (Einevoll et al., 2013; Khawaja, Tsui & Pack, 2009; Liu & Newsome, 2006). Past EEG and LFP studies have found that activity in the gamma (and high-gamma) frequency band (i.e. from 30-200 Hz) to be associated with functional cortical activation and sensorimotor integration (Pesaran et al., 2002; Ray et al., 2008). However, the relationship between gamma LFP and the neuronal firing properties of local networks remains unclear (He, 2014; Ray & Maunsell, 2011) and in order for the LFP to aid in a better understanding of local neuronal activity, we need to extract which aspects of neural mass action it reflects (Berrens, Logothetis & Tolias, 2010).

AIMS AND HYPOTHESES

Principle Aim:

'What information is contained within the gamma-band LFP of motion-selective neurons?'

Aim 1:

Can motion direction and speed be decoded from the gamma-band LFPs of neurons in visual area MT of anaesthetised marmosets?

Hypothesis 1:

Motion direction and speed will be able to be decoded from the LFP of neurons in visual area MT of anaesthetised marmosets. That is, there will be a significant difference between the LFP power of neurons exposed to different direction and speed combinations, leading to decodability above chance level (1 combination/60 combinations = 1.6% chance level).

Aim 2:

How does decodability (of MT neuron's stimulus selectivity) change when different LFP features are selected? (Such as averaging across time or the frequency bands, removing spikes from the raw LFP signal before decoding or differences between the initial and sustained components of the LFP power spectrum). And what can we infer about the information contained within the LFP?

Hypothesis 2:

Decoding accuracy percentages will be significantly different between groups with different features of the LFP selected. Firstly, any differences between the LFP when averaged across the time window or the frequency bands may be indicative of the points in time where most information is carried and which frequency bands contribute most to the stimulus selectivity. Secondly, removing spikes from the raw LFP signal before decoding will allow for identification of the contribution of spikes to the LFP signal and other components or cellular signalling methods that may have previously been hidden by the spiking pattern. Finally, comparing the decodability of the stimulus evoked initial and sustained components of the LFP will allow for the identification of which frequency band is most informative at different stages of cortical processing.

PROPOSED METHODOLOGY:

To address my research question I will be analysing extracellular microelectrode recordings from the middle temporal visual area (MT) in one adult male marmoset (*Callithrix jacchus*). The procedures used for this multi-unit recording in the anaesthetised, paralysed marmoset are the same as those used in previous studies within the Physiology Department of Monash University (Bourne & Rosa, 2003). Briefly, after being anaesthetised, a durotomy and

craniotomy were performed to allow for the insertion of the 96-microelectrode array in area MT. The monkey's pupils were dilated with topical atropine and the eye protected and focused at the desired viewing distance with contact lenses.

Visual Stimuli

Visual stimuli were monocularly presented and the eye ipsilateral to the recording site was occluded. Stimuli were presented on a View Pixx VPixx screen and generated using MATLAB (Mathworks, Natick, MA) and the Psychophysics Toolbox extensions. Stimuli consisted of a full screen of coherently moving white dots (randomly selected from one of 12 equally spaced directions around 360°; and at one of 5 randomly selected speeds from 5°, 10°, 20°, 40° or 80° of visual angle/sec) on a black background with a screen width of 520 mm and viewing distance of 300 mm (Figure 1). Stimuli were presented for 500 ms before a 500 ms interstimulus blank period. Monkeys viewed each of the sixty direction and speed combinations 60 times during a one hour testing period.

Fig. 1 - Schematic representation of the temporal sequence of our experimental stimulation. Monkeys were exposed to 500ms of stimulus motion in one of twelve equally spaced directions around 360° (i.e. from 0° to 330° in increments of 30°) and at one of five speeds (i.e. 5°, 10°, 20°, 40° or 80° visual angle/per second). Stimuli were presented for 500 ms before a blank interstimulus period of 500 ms. Monkeys viewed each of the sixty direction and speed combinations 60 times during a one hour testing period.

Analysis of Local Field Potentials

I will be using Matlab R2014a to analyse the microelectrode array data using scripts built in-house. Spike counts (the total number of action potentials) for each neuron are to be calculated individually based on time-logged stimulus presentation intervals across the duration of the experiment. From this, the local field potentials (LFPs) around each of the 96 microelectrodes will be calculated for every combination of direction and speed of stimulus motion.

Spectrograms showing the power of each neuron's signal per direction and speed (D/S) combination across the time and frequency domains will allow for visual identification of regions of interest (ROIs; time and frequency windows) to be later used for decoding. Based on past empirical evidence, we suggest this region will incorporate the gamma (and high-gamma) frequency band that has been shown to be involved in sensory integration (Crone, Sinai & Korzeniewska, 2006; Ray et al., 2008; Ray & Maunsell, 2011).

Decoding of the LFPs for viewed stimulus motion direction and speed will involve the use of our selected ROIs as 'classifier' patterns to be fed into a linear support vector machine (SVM) decoder algorithm. Here, a prediction of which D/S combination elicited which LFP response within a single trial will be reported using a confusion matrix (EXAMPLE FIG?) showing the percentage of correct decoding predictions ('hits') (Esghaei & Daliri, 2014; King & Dehaene, 2014). Furthering this, I will examine how decoding accuracy changes when different features of the LFP within the ROI are selected. This will include, for example, averaging across the time or frequency bands, removing the electrical contributions of spikes from the raw LFP signal before decoding and/or the inclusion of the LFP activity of neuron's without a direction or speed preference. Ultimately, I want to explore what information is contained within the gamma-band LFP of individual neurons in visual area MT and how this may translate to a better understanding of visual cortical network computations.

DATA ANALYSIS PLAN:

Proposed data analysis plan including statistics.

	ANALYSIS PLAN	STATISTICS
Pre-Processing: Determine the 'selectivity' of each neuron's LFP to every direction and speed combination to find that neuron's 'preference'	• Isolate individual neuron's LFPs to all D/S combinations • Find Z-score per D/S combination to determine neuron's 'preferred' D/S • Create spectrogram for each neuron's D/S combination to allow for the selection of the ROI (use same ROI for all neurons)	• Z-scores per direction and speed combination to find neuron's 'preference.
Hypothesis 1: There will be a significant difference between the LFP power of neurons exposed to different direction and speed combinations, leading to decodability above chance level	• For all neurons under the same D/S conditions, create vectors of the signal power from the ROI's time and frequency window • These vectorised signal power will then be used as input for the SVM decoder algorithm: with 70% used as the 'training' *classifier* pattern and 30% as the 'test' pattern • Returned is a percentage value of decoding accuracy (= correct hits)	• t-test comparing the accuracy of the decoder against the decoding chance level (1.66%)
Hypothesis 2: Decoding accuracy will be significantly different between groups with different features of the LFP selected	• Using the same methodology as above: the way in which the LFP ROI data is analysed/extracted will be altered to give a different *classifier* pattern for the decoder • Different analysis conditions: – Average across time – Average across frequency bands – Remove spike contribution from the raw LFP signal before analysis – Use only the initial component of the evoked LFP response (eg. first 100ms from stimulus onset) – Use only the sustained component of the evoked LFP response (eg. from 100-500ms from stimulus onset) – Include neurons with 'weak' D/S preferences – Selection of ROIs outside of the gamma-band frequency range	• ANOVA comparing the decoding accuracy between each group (with different features selected/ extracted). • ANOVA comparing each group against chance level (1.66%)

FEASIBILITY:

Feasibility of the project including the proposed timeline of research thesis completion and identification of any potential issues and how these may be addressed.

Proposed Timeline of Research Thesis: (OPTIONAL)

	April	May	June	July	August	Sept	Oct
Submit ethics, risk assessment and research proposal							
Data Analysis (exploring the LFP)							
Finish literature review (For use as introduction to thesis)							
Data Analysis (statistics) and preparation of figures							
Preparation of methods, results and discussion for thesis							
Finalisation of first draft of thesis							
Finalisation and presentation of research poster							
Finalisation and submission of research thesis							

Potential Issues and Remedies:

POTENTIAL ISSUES	SOLUTIONS
Data Issues: • Errors in the recording and labelling of the electrode microarray • Missing data • Too little data (and statistical power) recording from only one marmoset • Other data errors not yet specified	• Seek clarification of the recording conditions from Physiology department • Comparison of data set with Physiology department recording • Record data from a new marmoset (one month wait minimum)
Time Issues: • Increased processing time for data analysis and statistics • Interruptions to computational power (eg server down or hardware/software issues) • Mistakes in coding leading to incorrect and/or inaccurate results	• Ensure proposed timeline allows for at least one week per month of 'catch-up' time • Ensure proposed timeline deadlines are strictly adhered to • Write codes/scripts to maximise efficiency and minimise potential for errors
Analytical Issues: • Null results (or unexpected/ unanticipated) • Completion of data analysis ahead of schedule	• Explore all potential research avenues • Use null or unexpected results to shed light on other issues related to the research question • Follow up these results with further analyses and introduce new research questions
Theoretical Issues: • Increased time required to write thesis • Issues with literature review and investigation in past empirical research • Issues with write up and presentation of figures and tables	• Ensure proposed timeline allows for at least one week per month of 'catch up' time • Ensure proposed timeline deadlines are strictly adhered to • Use any 'downtime' periods to finish written sections of the thesis • Allow enough time to produce a number of drafts to be updated throughout the year

SIGNIFICANCE AND INNOVATION

In contrast to spike based neuronal output, the LFP measures the axonal and dendritic firing dynamics (input and output) of cortical network computations (Berrens, Logothetis & Tolias, 2010). However, the components comprising the component-selective gamma-band LFP signal and their contribution to local microcircuits remains to be elucidated (Einevoll et al, 2013; Khayat, Niebergall & Martinex-Trujillo, 2010; Liu & Newsome, 2006; Pesaran et al., 2012). Traditionally, studies of the visual system have relied on the use of spike counts, instead of the LFP, to determine stimulus-selectivity (Zanos, Mineault & Pack, 2011). In the few studies that have investigated the role of the LFP, the contributions of neurons that were not 'tuned' to stimulus properties were discarded and the spiking influence on the LFP was not removed from the raw signal (Khawaja, Tsui & Pack, 2009; Liu & Newsome, 2006). Both of these methodological issues have led to overestimation of the LFP power and a reduction in our ability to understand the contributions of the LFP to neural network processes (Pesaran et al., 2002; Zanos et al., 2011). The suggested role of these neurons ranges from regulation of contrast gain, the control of attention or a normalisation of outputs (Khawaja, Tsui & Pack, 2009) and in order for the LFP to aid in a better understanding of local neuronal activity, we need to extract the distinct information-carrying aspects of neural mass action it reflects (Berrens, Logothetis & Tolias, 2010).

To aid in this process, I have selected the use of SVM linear decoding – a novel process used to extract informational patterns and allow predictions of which neuronal responses were elicited by which experimental conditions (Eshgaei & Daliri, 2014). By comparing how decoding changes through the selection of different LFP components we may be better able to extricate the different functional mechanisms of the LFP signal and shed light on the computational dynamics within the visual system (Hung et al., 2005; Ince et al., 2010). Furthermore, elucidation of the neurophysiological mechanisms responsible for the high-gamma LFP response across cortical domains could allow for characterisation of the rate- and temporal-coding of cognitive processing and computations (Crone, Sinai & Korzeniewska, 2006; Ray et al., 2008). This increased understanding of the neural processes that the high-gamma LFP reflects has great clinical and research applications; allowing for the use of non-invasive electroencephalography (EEG) and magnetoencephalography (MEG) for the recording of LFPs and possible identification of dysfunctional processing in human subjects without requiring surgical implantation of electrode arrays (Einevoll et al., 2013; Crone, Sinai & Korzeniewska, 2006; He, 2014; King & Dehaene, 2014; Ray et al., 2008).

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