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Extraction of the average and differential dynamical response in stimulus-locked experimental data

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Abstract

In optical imaging experiments of primary visual cortex, visual stimuli evoke a complicated dynamics. Typically, any stimulus with sufficient contrast evokes a response. Much of the response is the same regardless of which stimulus is presented. For instance, when oriented drifting gratings are presented to the visual system, over 90% of the response is the same from orientation to orientation. Small differences may be seen, however, between the responses to different orientations. A problem in the analysis of optical measurements of the response to stimulus in cortical tissue is the distinction of the 'global' or 'non-specific' response from the 'differential' or 'stimulus-specific' response. This problem arises whenever the signal of interest is the difference in response to various stimuli and is evident in many kinds of uni- and multivariate data.

To this end, we present enhancements to a frequency-based method that we previously introduced called the *periodic stacking* method. These enhancements allow us to separately estimate the dynamics of both the average signal across all stimuli (the 'global' response) and deviations from the average amongst the various stimuli (the 'stimulus-specific' response) evoked in response to a set of stimuli. We also discuss improvements in the signal-to-noise ratio, relative to standard trial averaging methods, that result from the data-adaptive smoothing in our method.

Keywords: Optical imaging; Harmonic analysis; Spectral analysis; Global response; Differential response; EEG; Visual cortex; Trial averaging

1. Introduction

Experimental data of the dynamical response of a noisy system to a stimulus typically consist of repeated measurements of the response of the system to one or more stimuli. The challenge of analyzing such data lies in extracting the part of the measured signal that contains the response from background noise. Background noise, in this case, can mean true random noise, but can also mean any part of the signal that is not in response to the stimulus and therefore has a random phase with respect to the stimulus.

Here, we present a method to distinguish the dynamics of the average response from deviations away from the average due to differences between the stimuli. In the following, we will refer to the signal which represents deviations from the average as the *differential signal*. When responses to multiple stimuli are measured, there is an average dynamical response which is common to all stimuli. In many datasets that we study, the average response contains most of the power. We are typically interested in the differential response amongst the various stimuli. In particular, in optical imaging data of the intrinsic signal, the columnar structure of the response to oriented drifting gratings is only evident in the differential response. However, the average response contains 100 times the power (10 times the signal amplitude) of the differential response. If these two aspects of the signal are not accurately estimated and extracted from the data, it can significantly contaminate the differential signal.

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The most common method for increasing the signal-to-noise ratio for stimulus-response data is to average repeated measurements of the response, a method called trial averaging; this increases the signal-to-noise ratio by a factor of $\sqrt{M}$, where M is the number of repeated measurements. In this paper, we make use of a more powerful method that we call *periodic stacking* for extracting the response from noisy data based on signal characteristics in frequency space.

The underlying explanation for increased signal-to-noise ratio with periodic stacking is accurate identification of statistically significant sinusoids in the data. A powerful feature of this method is the elimination of inadmissible frequencies. This is augmented by the use of multitaper harmonic analysis (Thomson, 1982; Mitra and Pesaran, 1999). Although it is not commonly thought of in this respect, trial averaging methods indiscriminately include all sinusoids with the appropriate base frequency in the estimate of the periodic signal without checking for statistical significance, therefore a substantial amount of spurious noise can enter the signal estimate. By retaining only statistically significant harmonics in the estimate of the response, we reduce the effective number of degrees-of-freedom in our estimate of the signal resulting in a data-adaptive smoothing method.

2. Methods

First, we describe the periodic stacking method as applied to multiple measurements of the response to a single stimulus (Sornborger et al., 2003). Then we extend the method to the case of multiple measurements of the responses to multiple stimuli. To explain the simple underlying idea, we assume all responses $r_m(t)$ defined for $0 < t < T$ are of equal duration and concatenate all the M responses to a given stimulus.

The resulting function, of duration MT, we denote by $R(t)$. We define

$$R(mT + t) \equiv r_m(t) \tag{1}$$

where $r_m(t)$ is the response to the mth repetition of the stimulus, of duration T. Since we are measuring M responses to the same stimulus, the signal $R(t)$ is a combination of a T-periodic piece and measurement noise ϵ

$$R(t) = \sum_k \alpha_k\, \mathrm{e}^{2\pi ikt/T} + \epsilon(t) \tag{2}$$

where k is an integer. To understand the structure of the signal in Fourier space, we perform a Fourier transform on the signal. The Fourier transform $\beta(f)$ is given by the expression

$$\beta(f) = \frac{1}{MT}\int_{-MT/2}^{MT/2} \mathrm{e}^{-2\pi ift} R(t)\,\mathrm{d}t. \tag{3}$$

Inserting (2) into this expression and evaluating the integral on the periodic piece gives

$$\beta(f) = \sum_k \alpha_k \frac{\sin(MT\pi(k/T - f))}{MT\pi(k/T - f)} + \tilde{\epsilon}(f). \tag{4}$$

where $\tilde{\epsilon}(f)$ indicates the Fourier transform of the noise ϵ. In the limit of infinite data, this expression becomes (up to a normalization factor)

$$\beta(f) = \sum_k \alpha_k \delta(k/T - f). \tag{5}$$

From this expression, we see that the signal is a sequence of harmonics $\{\alpha_k\}$ at frequencies $f = k/T$.

Knowing the location and complex amplitude of the harmonics which carry the response and their statistical significance is the key to an accurate estimation of the signal. The above discussion considered a finite duration, continuous signal. To obtain an estimate of the harmonic amplitudes, $\{\alpha_k\}$, in noisy data, we must invert Eq. (4). Our data is discretely sampled. Therefore, to estimate the complex amplitude α_k of each harmonic, we use multitaper harmonic analysis (Thomson, 1982). Multitaper harmonic analysis seeks a solution to the inverse problem that is *local* in the frequency domain. This high-resolution method allows us to accurately determine the amplitude and phase of the periodic response and also gives an estimate of the noise and the statistical significance of deterministic sinusoids in a signal. Although we consider multitaper harmonic analysis to be the best, other, for instance, parametric harmonic detection methods could be used as well. Using multitaper harmonic analysis, we identify and extract the statistically significant sinusoids in the data which lie at multiples of the base frequency. Response contributions not located at frequencies commensurate with the base frequency are discarded as noise. We recombine the estimated sinusoids, thereby forming an estimate of the dynamical response.

The single stimulus analysis can be directly extended to the case of multiple stimuli. This is achieved by concatenating responses to N stimuli, each of duration T, resulting in a total stimulus period of duration NT. We acquire M measurements of responses to the N stimuli, resulting in a signal of length MNT. Thus, if $\rho_{mn}(t)$, $0 < t < T$ denotes the response in the mth repeat of the nth stimulus, we can define

$$R(mNT + nT + t) \equiv \rho_{mn}(t) \tag{6}$$

for $0 < t < T$, $m = 0, \ldots, M-1$ and $n = 0, \ldots, N-1$.

To understand the structure of this signal in Fourier space, we proceed similarly to the above discussion of the single stimulus case. The signal $R(t)$ can be expressed as an NT-periodic piece plus measurement noise,

$$R(t) = \sum_k \alpha_k\, \mathrm{e}^{2\pi ikt/NT} + \epsilon(t). \tag{7}$$

From the arguments in the previous section, the NT-periodic part of this signal lies at frequencies $f = k/NT$, where k is an integer. The Fourier transform of the signal is

$$\beta(f) = \frac{1}{MNT}\int_0^{MNT} \mathrm{e}^{-2\pi ift} R(t)\,\mathrm{d}t. \tag{8}$$