NOTE **Communicated by Jonathan Victor**

Spike Count Correlation Increases with Length of Time Interval in the Presence of Trial-to-Trial Variation

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It has been observed that spike count correlation between two simultaneously recorded neurons often increases with the length of time interval examined. Under simple assumptions that are roughly consistent with much experimental data, we show that this phenomenon may be explained as being due to excess trial-to-trial variation. The resulting formula for the correlation is able to predict the observed correlation of two neurons recorded from primary visual cortex as a function of interval length.

1 Introduction

Simultaneously recorded cortical neurons often exhibit correlations in spike counts over substantial periods of time, and this has been interpreted as producing important limitations on capacities for neural coding (Shadlen & Newsome, 1998; Zohary, Shadlen, & Newsome, 1994). However, it has also been observed that spike count correlations decrease as the length of the time interval decreases (Averbeck & Lee, 2003; Reich, Mechler, & Victor, 2001). We provide here a simple theoretical explanation of this phenomenon as a necessary consequence of excess trial-to-trial variation. The purposes of this work are two: first, to emphasize the importance of specifying interval length when interpreting spike count correlation, and, second, to focus further attention on excess trial-to-trial variation as an indicator of common neuronal input.

2 Results

Our object is to analyze the correlation of a pair of spike counts across repeated trials in the presence of excess trial-to-trial variability, under reasonable assumptions, when the measurement interval—and therefore each expected count—increases. Let us consider random variables Y_r^1 and Y_r^2 representing theoretical spike counts over an interval of length T for two

neurons recorded simultaneously on trial r. To simplify some formulas, we assume the two spike count probability distributions are the same, but this does not affect the essence of the result. We will also assume the following:

1. Within trials, the expected spike counts increase proportionally to T.
2. The within-trial variance is proportional to the within-trial expectation.
3. After conditioning on the trial, Y_r^1 and Y_r^2 are independent.

Assumptions 1 and 2 are roughly consistent with many observed data (see Shadlen & Newsome, 1998, for references). Assumption 1 concerns the within-trial expected spike counts. In the absence of excess trial-to-trial variation, the within-trial expected spike count would equal the trial-averaged spike count. When there is excess trial-to-trial variation, the neuronal response depends on some external or internal state S_r that varies with the trial. The within-trial expected spike count is the number that would be produced by, hypothetically, averaging spike counts over trials with identical values of the state S_r. Assumption 2 is much more general than the Poisson assumption, which would require the within-trial variance to equal the within-trial expectation. Assumption 3 eliminates short timescale effects and will be discussed below.

We also introduce a random variable X_r to represent excess trial-to-trial variation and will take the expectation of each spike count on trial r to be $f(X_r)$ when $T = 1$, for some function $f(x)$ (see equation 2.1 below). In the absence of excess trial-to-trial variation, $f(X_r)$ would be constant across trials.

2.1 Monotonically Increasing Correlation. Under these three assumptions, the correlation of Y_r^1 and Y_r^2 and the conditional expectation and variance of Y_r^i given the trial may be computed in terms of T. Before proceeding, we make two observations. First, under assumption 1, we may write the expectation conditionally on the trial effect X_r in the form

$$E(Y_r^i \mid X_r) = Tf(X_r), \tag{2.1}$$

where $f(X_r)$ becomes the expected spike count when $T = 1$. Second, under assumption 2, we may write

$$V(Y_r^i \mid X_r) = k \cdot E(Y_r^i \mid X_r),$$

and combining this with equation 2.1, we have

$$V(Y_r^i \mid X_r) = kTf(X_r). \tag{2.2}$$

In the case of Poisson counts, we would have $k = 1$. Underdispersion occurs when $k < 1$ and overdispersion when $k > 1$.

In computing the correlation of Y_r^1 and Y_r^2 we will use equations 2.1 and 2.2 together with elementary formulas for the variances and covariance in terms of the conditional variances, covariance, and expectations. For $i = 1, 2$, we have

$$\begin{aligned} V(Y_r^i) &= E(V(Y_r^i \mid X_r)) + V(E(Y_r^i \mid X_r)) \\ &= E(kTf(X_r)) + V(Tf(X_r)) \\ &= kTE(f(X_r)) + T^2V(f(X_r)), \end{aligned}$$

and, applying assumption 3 and equation 2.1,

$$\begin{aligned} COV\left(Y_r^1, Y_r^2\right) &= E\left(COV\left(Y_r^1, Y_r^2 | X_r\right)\right) + COV\left(E\left(Y_r^1 \mid X_r\right), E\left(Y_r^2 \mid X_r\right)\right) \\ &= 0 + T^2V(f(X_r)). \end{aligned}$$

Writing $\mu = E(f(X_r))$ and $\sigma^2 = V(f(X_r))$, we therefore obtain

$$COR\left(Y_r^1, Y_r^2\right) = \frac{T^2\sigma^2}{kT\mu + T^2\sigma^2} = \frac{T}{T + \omega}, \tag{2.3}$$

where $\omega = k\mu/\sigma^2$. This shows that the correlation will increase monotonically as T increases and will vanish as $T \to 0$.

To see the implication of equation 2.3, suppose that the trial-to-trial variation takes the form

$$E\left(Y_r^i \mid X_r\right) = Tf(X_r) = Tce^{X_r},$$

where c is the firing rate when $T = 1$ and $X_r = 0$, and, for simplicity, suppose further that X_r has a normal distribution. It is easily verified that if X_r has mean a and variance b^2, then

$$E\left(e^{X_r}\right) = e^{a+b^2/2}$$

and

$$V\left(e^{X_r}\right) = e^{2a+b^2}(e^{b^2} - 1).$$

These give the ratio

$$\frac{V\left(e^{X_r}\right)}{E\left(e^{X_r}\right)} = e^{a+b^2/2}\left(e^{b^2} - 1\right).$$

Using this formula, we may compute the correlation in equation 2.3 for various scenarios. For example, with a firing rate of $c = e^a = 20$ spikes per second and $b = 12.5\%$ trial-to-trial variation, correlations for counts in intervals of length 2 ms, 100 ms, and 1000 ms become .0006, .03, and .24, which are roughly consistent with those reported by Reich et al. (2001). We do not mean to suggest that trial-to-trial variation may be described well by normally distributed effects that are constant in time (see below). These values are provided, rather, to help interpret the predictions of equation 2.3.

2.2 Nonmonotonic Correlation. According to equation 2.3, the spike count correlation will increase monotonically and, furthermore, will approach 1 for sufficiently long time intervals. However, Averbeck and Lee (2003) report an increase of correlation as a function of T up to a maximum, and then a subsequent decline. We now show that such effects could also be due to excess trial-to-trial variability.

Suppose that the excess trial-to-trial variation is as described previously up to T_1, but that it disappears afterward. Such effects have been reported previously (e.g., Baker, Spinks, Jackson, & Lemon, 2001). Under assumptions 1, 2, and 3, when $T \le T_1$, equation 2.3 still applies. For $T > T_1$, we write $Y_r^i = Y_{r1}^i + Y_{r2}^i$, where Y_{r1}^i is the spike count in $[0, T_1]$, and Y_{r2}^i the spike count in $[T_1, T]$, for neuron i on trial r. Because the spike counts Y_{r2}^1 and Y_{r2}^2 in $[T_1, T]$ contain no excess trial-to-trial variation, they are mutually independent and are also independent from the spike counts Y_{r1}^1 and Y_{r1}^2 in $[0, T_1]$. Then, for $T > T_1$, we have

$$V(Y_r^i) = V(Y_{r1}^i) + V(Y_{r2}^i) = \left(k\ T_1\ \mu + T_1^2\ \sigma^2\right) + k(T - T_1)$$

and

$$COV(Y_r^1, Y_r^2) = COV(Y_{r1}^1, Y_{r1}^2) = T_1^2\ \sigma^2,$$

so that, for $T > T_1$,

$$COR(Y_r^1, Y_r^2) = \frac{T_1}{T_1 + w + \frac{k}{T_1\ \sigma^2}(T - T_1)}. \tag{2.4}$$

Under these conditions, the correlation will increase with T for $T < T_1$ and will decrease with T for $T > T_1$.

The modified assumption that trial-to-trial variability vanishes for $T > T_1$ is not supposed to reflect accurately a real situation. Rather, we have provided equation 2.4 to indicate possible nonmonotonic behavior. Other, more realistic forms of time-varying trial-to-trial effects could also produce correlations that are nonmonotonic in T. One relatively simple alternative

form of time-varying trial-to-trial variation is given, and its predictions are compared with data below.

2.3 Illustration with V1 Data. We illustrate using data from two neurons recorded simultaneously in the primary visual cortex of an anesthetized macaque monkey (Aronov, Reich, Mechler, & Victor, 2003, units 380506.s and 380506.u, 90 degree spatial phase), which were part of the Reich et al. (2001) study. Figures 1B and 1C show their peristimulus time histograms (PSTHs). Ventura, Cai, and Kass (2005) established that these two neurons had excess trial-to-trial variation, whose effects were shared across the neurons (see also Figure 1D), but that the neurons were independent once these effects were removed. Figure 1A displays the correlation of spike counts for increasing time intervals. The data for these two neurons were recorded from the same electrode, with an accuracy of 2.8 milliseconds, so that it was impossible to detect joint spikes occurring at time lags less than 2.8 milliseconds. This induces an artifactual negative correlation, clearly apparent in Figure 1A for the smallest time interval.

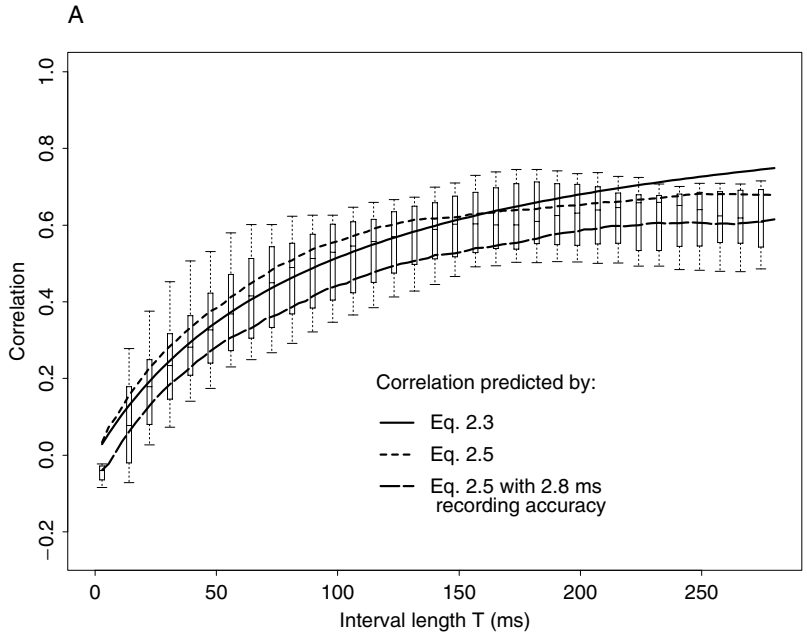
A fit of equation 2.3 to the data is overlaid in Figure 1A. It captures reasonably well the general trend of the correlation. However, it fails to follow a leveling off evident at intervals greater than about 200 milliseconds, which may be due to nonconstant trial-to-trial variation. Indeed, Ventura et al. (2005) showed that this pair of neurons had highly significant nonconstant trial-to-trial effects and that the firing rate of neuron i on trial r could be described better by the function

$$P_r^i(t) = P^i(t)\, e^{w_{0r}\phi(t)}, \tag{2.5}$$

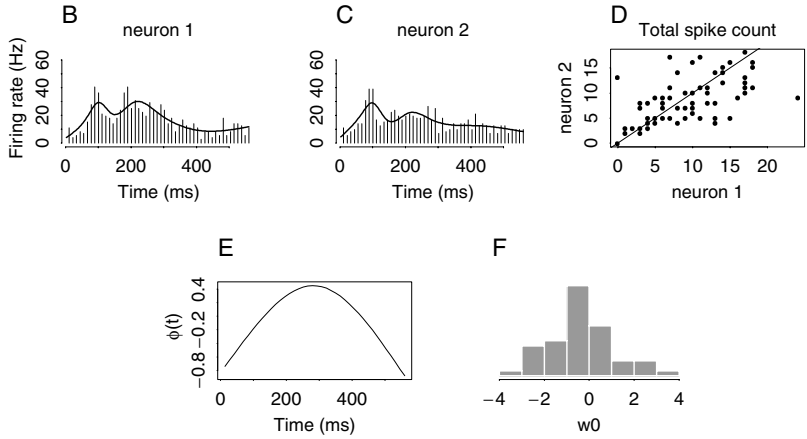
with $P^i(t)$ being the average firing rate of neuron i over many trials, and $w_{0r}\phi(t)$ being a nonconstant contribution shared across the two neurons. According to equation 2.5, the excess trial-to-trial variation is due to trial-specific effects w_{0r} that modulate the function $\phi(t)$. We could not produce analytical results, like those of equation 2.3, for the model of equation 2.5 because it is too complicated. Instead, we have calculated the predicted correlation curve by numerical simulation. We simulated 1000 pairs of spike trains from model 2.5 fitted to the data, which we used to compute the correlation as a function of interval length T.[1] We also adjusted the correlation function for the recording accuracy of 2.8 msec.[2] Figures 1B and 1C

[1] Specifically, we sampled with replacement 1000 values w_{0r}^* from the histogram in Figure 1F and then simulated pairs of Poisson spike trains with rates $P^i(t)e^{w_{0r}^*\phi(t)}$, $i = 1, 2$, with $P^i(t)$ and $\phi(t)$ shown in Figures 1B, 1C, and 1E.

[2] We identified all the occurrences of simultaneous spikes within 2.8 msec and, for each occurrence, retained the spike of only one neuron, chosen with probability proportional to its firing rate.



Data and fit of model in Equation 2.5



show estimates of $P^i(t), i = 1, 2$, taken to be the smoothed PSTHs, Figure 1E displays a fit of the function $\phi(t)$, and Figure 1F the histogram of the fitted trial-specific effect coefficients w_{0r}. In Figure 1A, the correlation predicted by equation 2.5 appears as the dashed curve, and the correlation after adjustment for the recording accuracy of 2.8 msec appears as the large-dashed curve. While equation 2.5 is itself a simplified representation of excess trial-to-trial variation and should not be expected to fit the data perfectly, these curves track the observed correlation quite well.

3 Discussion

Trial-to-trial variation is of interest not only for its physiological significance (Azouz & Gray, 1999; Hanes & Schall, 1996), but also because it confounds assessments of correlation (Brody, 1999a, 1999b; Ben-Shaul, Bergman, Ritov, & Abeles, 2001; Grün, Riehle, & Diesmann, 2003). We have shown here that excess trial-to-trial variation produces spike count correlations that vary with the length of time interval during which the counts are recorded. This follows, essentially, from assumptions 1 and 2 by formulas 2.1 and 2.2. When assumption 3 holds, monotonicity holds throughout the interval during which there is excess trial-to-trial variation and, furthermore, the correlation vanishes as $T \to 0$. We have also noted that when the excess trial-to-trial variation disappears after time T_1, the spike count correlation will decline after it reaches a maximum at an interval of length T_1. This behavior conforms to observations reported in Averbeck and Lee (2003). When there is correlation in the spike timing so that assumption 3 fails, it would be reasonable to assume, analogous to assumption 2, that the within-trial covariance between the two neurons' spike counts is proportional to

Figure 1: (A) Correlation between the spike counts for two neurons in primary visual cortex, as a function of interval length T. For each T, we plotted the box plot (quantiles and 10th and 90th quartiles) of the correlations obtained by sliding the interval along experimental time. The solid curve is equation 2.3 with $\omega = 34$. The dashed curve is the correlation function predicted by model 2.5 fitted to the data; the large-dashed curve is also for data as in equation 2.5 but with recording accuracy of 2.8 milliseconds to match the observed data. The activity of the two neurons was recorded during 64 trials from an anesthetized monkey; the stimulus in each trial was a standing sinusoidal grating that appeared at time 0 and disappeared at 237 ms. (B, C) Raw and smoothed PSTHs, $P^i(t)$, $i = 1, 2$, of the two neurons. (D) Within-trial spike counts for the complete interval of observation, which suggests that the neurons have shared effects of trial-to-trial variation. (E) The fitted firing rate modulating function $\phi(t)$ and (F) a histogram of the coefficients w_{0r}.

the within-trial expectation. We write:

$$COV\left(Y_r^1, Y_r^2 \mid X_r\right) = cTE\left(Y_r^1 \mid X_r\right). \tag{3.1}$$

In this case, monotonicity holds as long as $c < k$, and it is easy to show that $COR(Y^1, Y^2) \to c/k$ as $T \to 0$.

Note that in the absence of trial-to-trial variation, $f(X_r)$ becomes a constant, and under assumption 3, the spike counts are uncorrelated. If assumption 3 fails but equation 3.1 holds, in the absence of trial-to-trial variation, the correlation becomes constant and does not increase with the length of time interval. Under assumptions 1 and 2, an increase in spike count correlation with length of time interval, as in Figure 1A, is an indication of excess trial-to-trial variation that is shared across the two neurons. (For related methods and additional analyses of these data, see Ventura et al., 2005.)

We have offered our analysis in the usual spirit of those made with simplifying assumptions. We would not expect excess trial-to-trial variation to be summarized accurately by a single number, here represented as X_r. Ventura et al. (2005) have shown how somewhat more complicated phenomena involving trial-to-trial variability may be described. However, we would expect equations 2.3 and 2.4 to capture dominant effects, as illustrated in Figure 1A, and to provide insight into the possible origin of widely observed correlations.

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Received March 22, 2005; accepted April 14, 2006.