Spike Count Variability and the Poisson Hypothesis

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Abstract

The variability of cortical activity in response to repeated presentations of a stimulus has been an area of controversy in the ongoing debate regarding the evidence for fine temporal structure in nervous system activity. We present a new statistical technique for assessing the significance of observed variability in the neural spike counts with respect to a minimal Poisson hypothesis. We apply the method to recordings of inferotemporal cortical neurons of primates presented with complex visual stimuli, and report evidence suggestive of fine temporal structure occurring exclusively near the onset of presentation of the stimulus.

1 Introduction

The rate-coding hypothesis is roughly this: the *signal* embedded in a neural spike train is an underlying *rate*, varying on coarse time intervals on the order of several tens or hundreds of milliseconds; the rate in these intervals is reflected in the *number* of spikes which they contain. The precise placement of the spikes is random and immaterial. One of the phenomenona that bears on this controversy is the observed variability of *in vivo* cortical spike trains in response to repeated presentations of an identical stimulus. *If,* the reasoning goes, under identical conditions, when the neuron is presumably signalling the same event, the spike response varies, then the variations must be noise. This is, indeed, a reasonable *definition* of noise.

This argument is susceptible to a simple and familiar counterargument. Consider the following idealized model of a neuronal response during a 100 millisecond recording interval in response to, say, a bar of light in an identified receptive

field. Suppose that what the neuronal response actually encodes is in fact a far richer state space than the qualities of the bar of light, and involves other contextual elements such as the attentional state of the monkey, the past history of the neuron, the states of other neurons, other aspects of the visual stimulus, etc. (One could, quite reasonably, compile an unending list of such alternatives.) Now imagine that this larger state space contains exactly 2^{100} alternatives (the specific numbers are not important here), and furthermore that the neuron codes for them *exactly* deterministically, to within, say, 1 ms resolution: there is a one-to-one mapping between the state space and each of the 2^{100} possible spike trains. This neuron is notably a paradigm for the fine-temporal coding hypothesis. Now we present the bar several times. How does the neuron behave? Clearly, it depends on the probability distribution on the state space, or particularly, the probability distribution on the state space *conditioned* on presentation of the bar. For example, if we imagine that conditioned on presentation of the bar, all configurations of the state space are equally likely, then we would in fact observe, for the discretized spike train, a homogeneous Bernoulli process (with rate 1/2), the discrete cousin of the homogeneous Poisson process and the prototypical example of a temporally structureless stochastic process. Of course, from the perspective of physics, this has a familiar ring: it is difficult to meaningfully distinguish randomness induced by *our uncertainty* of the event (to be signalled) from the noise inherent in the (signalling) process.[1]

One statistic commonly employed to assay variability is the empirical mean-variance ratio of the spike counts (or its inverse, the Fano factor) across trials [Softky and Koch, 1993, Shadlen and Newsome, 1998, Tolhurst et al., 1983]. The spike counts of an inhomogeneous Poisson process are distributed as a discrete Poisson random variable, for which the mean and variance are identical. Thus observations of empirical mean-variance ratios near unity have led some to argue that neural spike trains are Poisson or Poisson-like processes [Softky and Koch, 1993, Tolhurst et al., 1983]. Of course, this does not itself reflect one way or another on the *fine-temporal vs. rate-coding* issue: determining whether fine-temporal coding is incompatible with observations of coarse-temporal structure is an interpretation requiring judgement of the cell's relationship to potentially hidden events. In one sense, this only increases our awareness of the difficulties involved in addressing the rate coding hypothesis.

In this light, *evidence* of finer temporal structure, particularly further away from direct sensory stimulation as in cortex, is particularly intriguing. Recently, Muller et al. [Muller et al., 2001] have observed, from recordings of V1 cells in primates presented with sinusoidal gratings, that near stimulus onset the empirical mean-variance ratio is strikingly higher than unity (in contradiction to the Poisson hypothesis). Our purpose in this note is twofold. First, we present evidence consistent with that of Muller et al., gathered here in cells from anterior IT of primates presented with more complex visual stimuli, of high mean-variance ratios particularly near stimulus onset. Secondly, we argue that the magnitude of the observed mean-variance ratios suggests that the spike processes cannot even be explained as samples from *non-repeating,* independent inhomogeneous

[1] Neuroscientists have, of course, worried about this for some time, [Gur et al., 1997].

Poisson processes, a more general class of processes, which includes the *mixtures* of inhomogeneous Poisson (or Cox) processes explored in the above thought experiment. We present an exact hypothesis test which quantifies this idea, apply it to this data, and, finally, speculate on the implications of this analysis.

2 Methods

2.1 Single Cell Recordings

Individual neurons from two monkeys (*macaca mulatta*) were isolated while the animals performed a basic fixation task. Surgical methods and chamber placement are described in Sheinberg and Logothetis (1997; 2001) . The activity of each cell was recorded while the monkey maintained fixation within a region 2 degrees square. Stimuli were approximately 4 degrees on a side. None of the stimuli were ever designated as special to the monkeys prior to training, although the test set did include pictures of human faces and other monkeys, as well as hundreds of other animals and man made objects. Each cell was tested with at least eight stimuli, but often with many more (up to 80). Stimuli were presented for either 800 or 1100 ms during which time the monkey was not allowed to look outside the virtual fixation window or the trial would automatically abort.

2.2 A Statistical Test

Consider a series of spike trains from a single neuron obtained from n separate trials (each involving, for example, presentation of the same stimulus):

$\{t_1^1, t_2^1, t_3^1, ..., t_{m_1}^1\}, \{t_1^2, t_2^2, t_3^2, ..., t_{m_2}^2\}, ..., \{t_1^n, t_2^n, ..., t_{m_n}^n\},$

where there are m_j spikes in trial j, and t_i^j is the time of occurrence of the i'th spike in the j'th trial, relative to a stimulus onset at time 0.

Our null hypothesis (H_0) is that $m_1, m_2, ..., m_n$ are independent Poisson random variables.[2] Let us designate the (unknown) rates as $\lambda_1, \lambda_2, ..., \lambda_n$. Define the empirical mean and variance statistics as usual:

$$\hat{\mu} := \frac{1}{n}\sum_{i=1}^{n} m_i \qquad \hat{\sigma}^2 := \frac{1}{n-1}\sum_{i=1}^{n}(m_i - \hat{\mu})^2$$

We seek a hypothesis test under our null which has power when $\hat{\mu}/\hat{\sigma}^2$ is large, or more to the point, such that $\hat{\sigma}^2$ is small, given $\hat{\mu}$. One way to proceed is to form a partition of the sample space based on $\hat{\mu}$. We seek $f(\hat{\mu})$ such that

$$P\left(\frac{\hat{\mu}}{\hat{\sigma}^2} \geq f(\hat{\mu}) \middle| \hat{\mu}\right) \leq \alpha \quad \forall \hat{\mu} \quad \forall P \in H_0$$

Then the event $\{\hat{\mu}/\hat{\sigma}^2 \geq f(\hat{\mu})\}$ will be an α-level hypothesis test, since:

[2] This contains the null hypothesis that we suggested earlier as a special case, i.e., that for each i, $\{t_1^i, ..., t_{m_i}^n\}$ is a sample from an independent inhomogeneous Poisson process.

$$P\left(\frac{\hat{\mu}}{\hat{\sigma}^2} \geq f(\hat{\mu})\right) = \sum_{\hat{\mu}} P\left(\frac{\hat{\mu}}{\hat{\sigma}^2} \geq f(\hat{\mu}) \middle| \hat{\mu}\right) P(\hat{\mu}) \leq \sum_{\hat{\mu}} \alpha P(\hat{\mu}) = \alpha \quad \forall P \in H_0$$

To compute $f(\hat{\mu})$, note the algebraic relation

$$\left\{\frac{\hat{\mu}}{\hat{\sigma}^2} \geq k\right\} = \left\{\sum_{i=1}^{n} m_i^2 \leq (n-1)\left(\frac{\hat{\mu}}{k} + \frac{n}{n-1}\hat{\mu}^2\right)\right\}.$$

Then it straightforward to apply the following proposition, which we state here without proof.

Proposition. *If $m_1, m_2, ..., m_n$ are independent Poisson random variables with rates $\lambda_1, \lambda_2, ..., \lambda_n$, respectively, then for all r, and for all $\hat{\mu}$, we have*

$$\max_{\lambda_1, \lambda_2, ..., \lambda_n} P\left(\sum_{i=1}^{n} m_i^2 \leq r \middle| \hat{\mu}\right) = \text{Prob}\left(\sum_{i=1}^{n} X_i^2 \leq r\right)$$

where $X_1, X_2, ..., X_n$ are distributed multinomially with parameters $\{n\hat{\mu}; 1/n, 1/n, ..., 1/n\}$.

Thus we have

$$\begin{aligned} f(\hat{\mu}) \quad := \quad & \max\left\{k : \text{Prob}\left(\sum_{i=1}^{n} X_i^2 \leq (n-1)\left(\frac{\hat{\mu}}{k} + \frac{n}{n-1}\hat{\mu}^2\right)\right) \leq \alpha\right\} \\ & \text{where} X_1, ..., X_n \sim \mathcal{M}(n\hat{\mu}; 1/n, 1/n, ..., 1/n) \end{aligned}$$

There are at least two practical ways to compute the multinomial probability associated with f. It can be computed exactly, as we do below, by dynamic programming [Bellman, 1957], if $\sum_{i=1}^{n} m_i$ and $\sum_{i=1}^{n} m_i^2$ are not too large, or it can be computed approximately, by Monte Carlo methods.

3 Results

We divided the one second period following stimulus onset into epochs, consisting of disjoint intervals. We used intervals of length 100 ms, 50 ms, and 25 ms. For each cell-simulus pair in our data set, we assessed the significance of our hypothesis test as outlined above. To assess the significance of the *number* of rejections of the null hypothesis (across cell-stimulus pairs) at 95% significance, we used a standard binomial test, assuming that the likelihood of rejecting the null was 5%, and independence of tests (Figure 1). We conclude that we can reject the null hypothesis that spikes are Poisson (in our general sense) near stimulus onset. Oddly, by examining finer epochs, we observe that we can reject the null hypothesis in the particular time period from 175 to 200 milliseconds following stimulus onset.

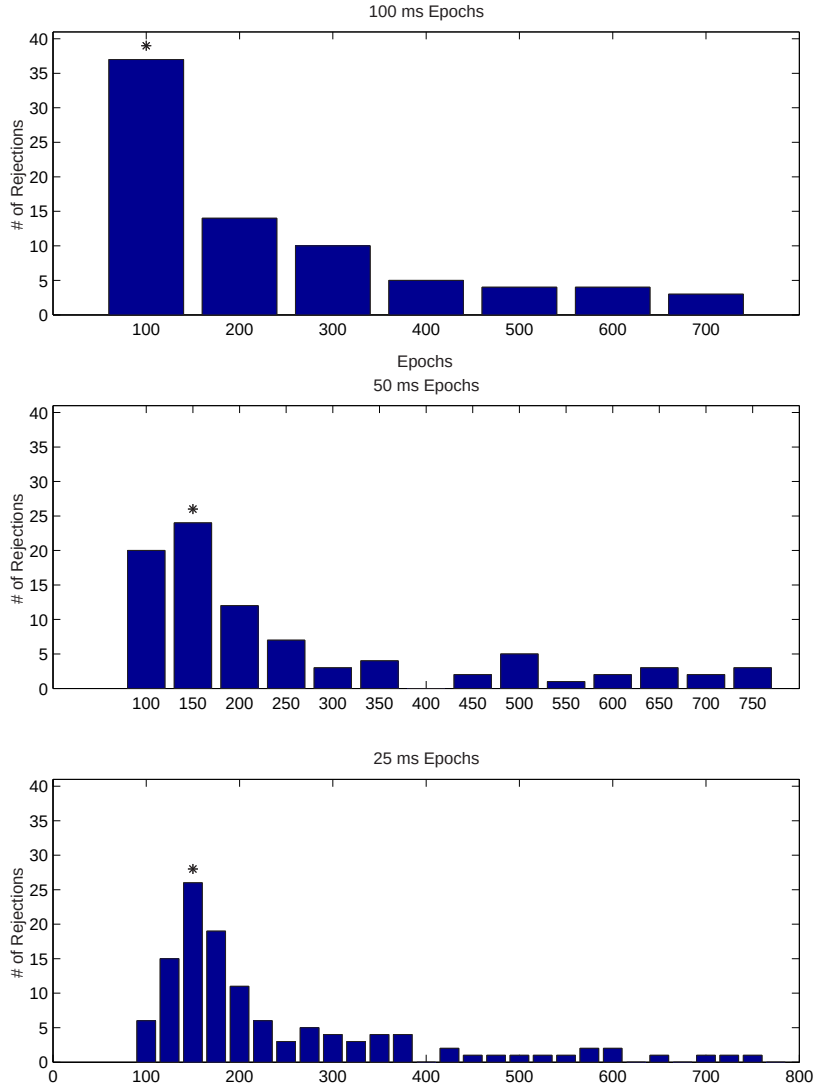

Figure 1: Number of rejections across a total of 301 cell-stimulus pairs for each epoch. The 800 milliseconds following stimulus onset were partitioned into disjoint intervals called epochs. Epochs are labelled along the x-axis by the starting time of the interval with which they are associated. Starred bars indicate a significant number of rejections ($p < .05$), as assessed by the binomial test (see text). The p-values associated with the significant epochs above are 10^{-6}, 0.017, and 0.0152, for the top, middle, and bottom graphs, respectively. The number of trials available for a single cell-stimulus pair ranged from 2 to 14, with a mean of 7.

4 Conclusion

We presented a novel statistical method which tests the general Poisson hypothesis against an alternative of repeatability in neural spike counts. Applying this technique to data from inferotemporal cortical neurons, we were able to reject this hypothesis. From a certain perspective, of course, this is not altogether that surprising: well-known biophysical properties of neurons such as bursting and the refractory periods alone might lead us to suspect that neural behavior is not strictly describable by Poisson-style models. However, because this test is designed to be optimal against an alternative of *too little* variability, it is reasonable to hypothesize that this rejection is about the repeatability of the neural response, rather than such internal effects in and of themselves. In this light, it is interesting that i) we are able to reject the hypothesis near stimulus onset, and not further away, and that ii) we are able to focus the locus of our rejection in small temporal intervals, despite grouping across many cells and stimuli, and despite having made no attempt to align latencies to the firing profiles of individual cell-stimulus pairs.

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