Analytical Models of Firing Rate Statistics in Sensory Neuroscience Experiments

Christopher C. Pack
Montreal Neurological Institute (MNI)
McGill University
Montreal, Quebec, Canada
e-mail: christopher.pack@mcgill.ca

Charles D. Pack
Computer Science Dept.
Monmouth University
Red Bank, NJ
e-mail: cpack@monmouth.edu

Abstract— **Motivated by empirical results, we develop simple Taylor Series approximations (analytics) for statistics associated with neuronal response data in sensory (e.g., vision) experiments in a laboratory setting. Such responses exhibit a non-negativity constraint and additional nonlinearities, such as "normalization". These transformations also change correlations among neuronal responses, which are thought to limit the fidelity of sensory representations. Simulation studies and cases, where we have exact results, show that our models are accurate over a wide range of parameter values. Ignoring constraints, simple analytical expressions help explain how data quality, parameter values and sensitivities affect results.**

Keywords*- data; measurements; analytics; statistics; simulation; neuroscience; vision experiments.*

I. INTRODUCTION

Many sub-disciplines within the field of brain science are concerned with the relationship between sensory (e.g., vision) stimuli and electrical activity in groups of neurons. The fidelity of this "neural code" is thought to depend on the firing rates of individual neurons and the variability or noise associated with these rates. Standard models of neural coding suggest that noise that is correlated across neurons deteriorates sensory representations in the brain [1]. Recent work has proposed that a specific transform operation, "normalization," might reduce the impact of correlated noise on neural coding. Support for this idea comes from simulations [2] and experimental observations. [3][4]. There are some analytical models for untransformed signal correlations [5][6]. Here, we develop new analytical models of pairwise correlations in neural responses to multiple replications of various sensory stimuli as well as the parametric relationship between a common nonlinear transformation and noise correlations. While we obtain some exact analytical results, degree-2 Taylor Series (T-S) approximations are particularly useful for transformed responses that require non-negativity constraints. Simulations show that our approximations are quite accurate for parameter values of interest to neuroscientists, but can be inaccurate or unstable at parameter extremes.

In Section II, we describe our neuroscience experiments, data/measurements and important statistics. In Section III, we develop some analytical models and Taylor-Series approximations. In Section IV, we provide analytical and simulation results. Section V contains a summary and important conclusions.

II. NEUROSCIENCE EXPERIMENTS, DATA, STATISTICS

In neuroscience experiments, data come from electrophysiological recordings of two (or more) neurons, during the presentation of a sensory stimulus such as a visual image. Each neuron fire spikes, which are discrete events that we measure over some time window. The measured spike counts are generally assumed to follow a Poisson distribution. We record these responses to *N* repetitions of the *M* different visual stimuli. For any stimulus, *i*, we have a pair of vectors ($\hat{\lambda}_{ij1}$, $\hat{\lambda}_{ij2}$), corresponding to the measured responses of the two neurons across repetitions of the same stimulus. From those, we calculate *rnoise(i)*, the correlation between these vectors. If we then take the mean, i.e., we "smooth" the original spike counts across repetitions, *j*, we get vectors ($\hat{v}_{i1}$, $\hat{v}_{i2}$). We next calculate the correlation between $\hat{v}_{i1}$ and $\hat{v}_{i2}$ to get a measure, *rsignal(i)*, of the stimulus preferences of the two neurons. Because of limited data, neuroscientists often compute, *rsignal~,* a "pseudo-correlation" over *M* stimuli. Finally, neuroscientists may analyze transformations of unsmoothed and smoothed responses with correlations *rnoise(i)'* and *rsignal~'*. We analyze statistics for our models of these four cases: 1. ($\hat{\lambda}_{ij1}$, $\hat{\lambda}_{ij2}$) *(rnoise(i));* 2. ($\hat{v}_{i1}$, $\hat{v}_{i2}$) *(rsignal~);* 3. Transformed responses ($\hat{\lambda}'_{ij1}$,$\hat{\lambda}'_{ij2}$) *(rnoise(i)');* 4. Transformed, averaged ($\hat{v}'_{i1}$, $\hat{v}'_{i2}$) *(rsignal~').* Cases 1-3 can be done exactly; Case 4 needs analytical approximations.

III. ANALYTICAL MODELS

We now develop analytical models for each of the four above cases.

A. Case 1: Original Data and rnoise(i)

For each neuron, *k = 1 or 2*, there are response measurements $\hat{\lambda}_{ijk}$=$\lambda_{ik}(1+\varepsilon_{ijk})$ corresponding to stimuli *i=1,…,M* and replications *j=1,…,N.* The λ_{ik} and ε_{ijk} are the "true" random spike counts and the independent random measurement error factors. Let $E(\lambda_{ik})=\bar{\lambda}_{ik}$ and $var(\lambda_{ik})=\sigma^2_{\lambda_{ik}}$. The correlation between the two neuron

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responses (signals) is $\rho(\lambda_{i1},\lambda_{i2}) \geq \rho(\hat{\lambda}_{ij1},\hat{\lambda}_{ij2})$. We assume ε_{ijk} is $N(0,\sigma_{\varepsilon_k}^2)$. It follows that $E(\hat{\lambda}_{ijk}) = \bar{\lambda}_{ik}$ and $var(\hat{\lambda}_{ijk}) = \sigma_{\lambda_{ik}}^2 + \bar{\lambda}_{ik}^2\sigma_{\varepsilon_k}^2 + \sigma_{\lambda_{ik}}^2\sigma_{\varepsilon_k}^2$. If measured responses are Poisson, $var(\hat{\lambda}_{ijk}) = E(\hat{\lambda}_{ijk}) = (\bar{\lambda}_{ik})$. Then, we have $cov(\hat{\lambda}_{ij1},\hat{\lambda}_{ij2}) = cov(\lambda_{i1},\lambda_{i2}) = \rho(\lambda_{i1},\lambda_{i2})\sigma_{\lambda_{i1}}^2\sigma_{\lambda_{i2}}^2$ and

$$rnoise(i) = \frac{cov(\hat{\lambda}_{ij1},\hat{\lambda}_{ij2})}{\sqrt{var(\hat{\lambda}_{ij1})var(\hat{\lambda}_{ij2})}} = \frac{\rho(\lambda_{i1},\lambda_{i2})}{\sqrt{(1+\bar{\lambda}_{i1}^2\frac{\sigma_{\varepsilon_1}^2}{\sigma_{\lambda_{i1}}^2}+\sigma_{\varepsilon_1}^2)(1+\bar{\lambda}_{i2}^2\frac{\sigma_{\varepsilon_2}^2}{\sigma_{\lambda_{i2}}^2}+\sigma_{\varepsilon_2}^2)}}. \quad (1)$$

Note that only the denominator involves measurement uncertainty. There is one unintended impact of the product-form analytical model for Case 1 (and Case 3, below). Given the *MxNx2* measurements from a vision experiment, we might use the common variance estimator for sample variances: $\sigma_{\hat{\lambda}_{ijk}}^2 = var(\hat{\lambda}_{ijk}) \approx \hat{\sigma}_{\hat{\lambda}_{ijk}}^2 = \frac{\sum_{j=1}^{N}(\hat{\lambda}_{ijk}-\frac{\sum_{p=1}^{N}\hat{\lambda}_{ipk}}{N})^2}{N-1} = \frac{\sum_{j=1}^{N}(\hat{\lambda}_{ijk}-\hat{v}_{ik})^2}{N-1}$, where $\hat{v}_{ik}$ is an estimate of $E(\hat{\lambda}_{ijk})$. The problem is that $E\left(\hat{\sigma}_{\hat{\lambda}_{ijk}}^2\right) = \sigma_{\hat{\lambda}_{ijk}}^2 - \sigma_{\lambda_{ik}}^2 \neq \sigma_{\hat{\lambda}_{ijk}}^2$. which is *biased low* for $var(\hat{\lambda}_{ijk})$ when $\hat{\lambda}_{ijk}$ is the product of 2 random variables. We will need to correct this bias in our simulation. Similarly, if we use the standard covariance estimator for $\hat{\varsigma}(i) \approx cov(\hat{\lambda}_{ij1},\hat{\lambda}_{ij2}) = cov(\lambda_{i1},\lambda_{i2})$, we get $\hat{\varsigma}(i) = \frac{\sum_{j=1}^{N}(\hat{\lambda}_{ij1}-\hat{v}_{i1})(\hat{\lambda}_{ij2}-\hat{v}_{i2})}{N-1}$, with the result that E[$\hat{\varsigma}(i)$]=0, which is *also biased low* and needs to be corrected in the simulation results.

B. Case 2: "Smoothed" Data and rsignal(i), rsignal~

Let $\hat{v}_{ik} = \frac{\sum_{j=1}^{N}\hat{\lambda}_{ijk}}{N} = \lambda_{ik}(1+\frac{\sum_{j=1}^{N}\varepsilon_{ijk}}{N})$ for *i=1,...,M*. Then, for all *i*, $E(\hat{v}_{ik}) = \bar{\lambda}_{ik}$, $var(\hat{v}_{ik}) = \sigma_{\lambda_{ik}}^2 + \frac{\bar{\lambda}_{ik}^2\sigma_{\varepsilon_k}^2}{N} + \frac{\sigma_{\lambda_{ik}}^2\sigma_{\varepsilon_k}^2}{N}$. Further, $cov(\hat{v}_{i1},\hat{v}_{i2}) = cov(\hat{\lambda}_{ij1},\hat{\lambda}_{ij2}) = cov(\lambda_{i1},\lambda_{i2})$, and correlation $rsignal(i) = \frac{cov(\hat{v}_{i1},\hat{v}_{i2})}{\sqrt{var(\hat{v}_{i1})var(\hat{v}_{i2})}} =$

$$\frac{\rho(\lambda_{i1},\lambda_{i2})\sigma_{\lambda_{i1}}\sigma_{\lambda_{i2}}}{\sqrt{\sigma_{\hat{v}_{i1}}^2\sigma_{\hat{v}_{i2}}^2}} = \frac{\rho(\lambda_{i1},\lambda_{i2})}{\sqrt{(1+\bar{\lambda}_{i1}^2\frac{\sigma_{\varepsilon_1}^2}{N\sigma_{\lambda_{i1}}^2}+\sigma_{\varepsilon_1}^2)(1+\bar{\lambda}_{i2}^2\frac{\sigma_{\varepsilon_2}^2}{N\sigma_{\lambda_{i2}}^2}+\sigma_{\varepsilon_2}^2)}} \quad (2)$$

Equation (2) is quite similar to (1) except that measurement error variances are divided by *N*. Then, due in part to data limitations, neuroscientists generally use (define) *rsignal~*, a different measure of the similarity of neuronal responses to various stimuli. That is, *rsignal~*

$$= \frac{cov\sim(\hat{v}_{*1},\hat{v}_{*2})}{\sqrt{var\sim(\hat{v}_{*1})var\sim(\hat{v}_{*2})}} = \frac{E\sum_{i=1}^{M}(\hat{v}_{i1}-\hat{v}_{*1})(\hat{v}_{i2}-\hat{v}_{*2})}{\sqrt{E\sum_{i=1}^{M}(\hat{v}_{i1}-\hat{v}_{*1})^2 E\sum_{i=1}^{M}(\hat{v}_{i2}-\hat{v}_{*2})^2}} \quad (3)$$

where $\hat{v}_{*k} = \frac{\sum_{i=1}^{M}\hat{v}_{*k}}{M}$. While $cov(\hat{v}_{i1},\hat{v}_{i2}) = cov(\hat{\lambda}_{ij1},\hat{\lambda}_{ij2})$, $cov\sim(\hat{v}_{*1},\hat{v}_{*2}) \neq cov(\hat{\lambda}_{ij1},\hat{\lambda}_{ij2})$. We can compute *rsignal~*, in terms of more traditional moments, using

$$E\sum_{i=1}^{M}(\hat{v}_{i1}-\hat{v}_{*1})(\hat{v}_{i2}-\hat{v}_{*2}) = \frac{M-1}{M}\sum_{i=1}^{M}\left[cov(\lambda_{i1},\lambda_{i2}) + \bar{\lambda}_{i1}\bar{\lambda}_{i2}\right] - \frac{1}{M}\sum_{i=1}^{M}\sum_{p\neq i}^{M}\left[cov(\lambda_{i1},\lambda_{p2}) + \bar{\lambda}_{i1}\bar{\lambda}_{p2}\right], \quad (4)$$

$$E\sum_{i=1}^{M}(\hat{v}_{ik}-\hat{v}_{*k})^2 = \frac{M-1}{M}\sum_{i=1}^{M}(\sigma_{\varepsilon_k}^2 + \bar{\lambda}_{ik}^2) - \frac{1}{M}\sum_{i=1}^{M}\sum_{p\neq i}^{M}\left[cov(\lambda_{ik},\lambda_{pk}) + \bar{\lambda}_{ik}\bar{\lambda}_{pk}\right]. \quad (5)$$

Assume inter-stimuli covariances in (4), (5) are negligible.

C. Cases 3 and 4: Transformed Responses

First, we define the normalization transformation that we use in this report:

$$\begin{aligned}\hat{\lambda}'_{ijk} &= f(\lambda_{ik},\lambda_{ik-},\varepsilon_{ijk},\varepsilon_{ijk-})\\ &= \max\left(0,\frac{\hat{\lambda}_{ijk}^2}{s\hat{\lambda}_{ijk}^2+c} - r\frac{\hat{\lambda}_{ijk-}^2}{s\hat{\lambda}_{ijk-}^2+c}\right)\\ &= \max\left(0, g(\lambda_{ik},\lambda_{ik-},\varepsilon_{ijk},\varepsilon_{ijk-})\right)\\ &= \max\left(0,\frac{[\lambda_{ik}(1+\varepsilon_{ijk})]^2}{s[\lambda_{ik}(1+\varepsilon_{ijk})]^2+c} - \frac{r[\lambda_{ik-}(1+\varepsilon_{ijk-})]^2}{s[\lambda_{ik-}(1+\varepsilon_{ijk-})]^2+c}\right)\end{aligned} \quad (6)$$

where *s, c, r* are non-negative constants and *k-* is the opposite neuron index from *k.* The first term in expanded (6) corresponds to the standard form of normalization used in neuroscience [7]; the terms in the denominator can be thought of as corresponding to pools of neurons that are correlated (first term) or uncorrelated (second term) with the neuron in the numerator. The second term in the equation allows for the possibility of opponent processing, a common neural operation that is hypothesized to influence noise correlations [8]. The max function captures the fact that neural firing rates cannot, by definition, be negative. We will see that the transformations in Cases 3 and 4 increase complexity because they:

- Are highly non-linear and may need to be *constrained* to be non-negative
- Add many parameters to the model
- Reduce the non-negative magnitude of the (transformed) responses, $\hat{\lambda}'_{ijk}$, to near 0
- Cause correlation statistics, such as *rnoise(i)'* and *rsignal~',* to become very sensitive to important system parameters, e.g., as $\hat{\lambda}'_{ijk}$ approaches 0.

In our simulation of Case 3, i.e., smoothed transformed data and *rnoise(i)'*, we have to correct biases in the *classic* variance and covariance estimators, $\hat{\sigma}_{\hat{\lambda}'_{ijk}}^2$ and $\hat{c}(\hat{\lambda}'_{ij1},\hat{\lambda}'_{ij2})$, for $var(\hat{\lambda}'_{ijk})$ and $cov(\hat{\lambda}'_{ij1},\hat{\lambda}'_{ij2})$. That is, for $j \neq p$:

$$E\left(\hat{\sigma}_{\hat{\lambda}'_{ijk}}^2\right) = var(\hat{\lambda}'_{ijk}) + E^2(\hat{\lambda}'_{ijk}) - E(\hat{\lambda}'_{ijk}\hat{\lambda}'_{ipk}) \quad (7)$$

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and

$$E\left(\hat{c}\left(\hat{\lambda}'_{ij1},\hat{\lambda}'_{ij2}\right)\right) = cov\left(\hat{\lambda}'_{ij1},\hat{\lambda}'_{ij2}\right) + E\left(\hat{\lambda}'_{ij1}\right)E\left(\hat{\lambda}'_{ij2}\right) - E\left(\hat{\lambda}'_{ij1}\hat{\lambda}'_{ip2}\right). \quad (8)$$

We also developed exact and T-S analytical models for Case 3. Our exact approach conditions on λ_{ijk} and λ_{ijk-} in (6), then assumes a joint distribution for them and integrates out to obtain expected values, variances and covariances for $\hat{\lambda}'_{ijk}$. The limits on the integrals reflect the non-negativity constraint. Our analytical approximations focus on degree-2 Taylor Series (TS-2) models (extensive empirical analyses show that the much more complex higher degree models "overfit" the data), with a differentiable approximation of the non-negativity constraint for $\hat{\lambda}'_{ijk}$ in (6). We use Taylor Series models because they often provide very good approximations and reveal critical statistical relationships between input parameters and results. We have not quantified the very small approximation errors. Important TS-2 moments, including correlations, are linear combination of input variances/ covariances, with weights being algebraic expressions of input parameters. Of special interest is the Simplified TS-2 (STS-2) version of the model that is valid when the non-negativity constraint is "non-binding". To develop the TS-2 Model, we replace the non-negativity constraint in the *f* form of (6) with

$$\hat{\lambda}'_{ijk} = f\left(\lambda_{ik}, \lambda_{ik-}, \varepsilon_{ijk}, \varepsilon_{ijk-}\right)$$

$$\approx \frac{g(\lambda_{ik},\lambda_{ik-},\varepsilon_{ijk},\varepsilon_{ijk-}) + \sqrt{g(\lambda_{ik},\lambda_{ik-},\varepsilon_{ijk},\varepsilon_{ijk-})^2 + \delta}}{2} \quad (9)$$

where δ, which is required for differentiability, is a very small positive number. Then, the Taylor Series fit to *f*, as given by (9), is around the "point" $(\bar{\lambda}_{ik}, \bar{\lambda}_{ik-}, \bar{\varepsilon}_{ijk}, \bar{\varepsilon}_{ijk-})$. We assume that the λ's have a bivariate Normal distribution with means $(\bar{\lambda}_{ik}, \bar{\lambda}_{ik-})$, variances $(\sigma^2_{\lambda_{ik}}, \sigma^2_{\lambda_{ik-}})$ and correlation $\rho(\lambda_{ik}, \lambda_{ik-})$. The ε's are each (independently) normally distributed with 0 means and variances $\sigma^2_{\varepsilon_k}$ *and* $\sigma^2_{\varepsilon_{k-}}$, respectively. Accuracy is usually best when variances $(\sigma^2_{\lambda_{ik}}, \sigma^2_{\lambda_{ik-}}, \sigma^2_{\varepsilon_k}, \sigma^2_{\varepsilon_{k-}})$ are small. To get the simpler STS-2 model results, we ignore the non-negativity constraint, i.e., $f \equiv g$. With limited space, we present some results. First, the TS-2 expression for the mean is:

$$E\left(\hat{\lambda}'_{ijk}\right) \approx f + \frac{1}{2}\left[f_{\varepsilon_{ijk}\varepsilon_{ijk}}\sigma^2_{\varepsilon_k} + f_{\varepsilon_{ijk-}\varepsilon_{ijk-}}\sigma^2_{\varepsilon_{k-}} + f_{\lambda_{ik}\lambda_{ik}}\sigma^2_{\lambda_{ik}} + f_{\lambda_{ik-}\lambda_{ik-}}\sigma^2_{\lambda_{ik-}}\right] + f_{\lambda_{i1}\lambda_{i2}}cov(\lambda_{i1},\lambda_{i2}) \quad (10)$$

In (10), the subscripts on *f* and *g* represent partial derivatives and all expressions in *f* and *g* are evaluated at the mean point $\left(\bar{\lambda}_{ik}, \bar{\lambda}_{ik-}, 0,0\right)$. Also, all of the partials, f_{xy}, are of the form:

$$f_{xy} = \frac{1}{2}\left[g_x g_y \frac{\delta}{(g^2+\delta)^{1.5}} + \left(1 + \frac{g}{\sqrt{g^2+\delta}}\right) g_{xy}\right] \quad (11)$$

with the following pairs for (x,y), with corresponding *g* partials (evaluated at mean):

- $(\varepsilon_{ijk}, \varepsilon_{ijk})$: $g_{\varepsilon_{ijk}} = \frac{2c\bar{\lambda}^2_{ik}}{[s\bar{\lambda}^2_{ik}+c)^2}$, $g_{\varepsilon_{ijk}\varepsilon_{ijk}} = \frac{2c\bar{\lambda}^2_{ik}(c-3s\bar{\lambda}^2_{ik})}{[s\bar{\lambda}^2_{ik}+c)^3}$ (12A)
- $(\varepsilon_{ijk-}, \varepsilon_{ijk-})$: $g_{\varepsilon_{ijk-}} = \frac{-2rc\bar{\lambda}^2_{ik-}}{[s\bar{\lambda}^2_{ik-}+c)^2}$, $g_{\varepsilon_{ijk-}\varepsilon_{ijk-}} \frac{-2rc\bar{\lambda}^2_{ik-}(c-3s\bar{\lambda}^2_{ik-})}{[s\bar{\lambda}^2_{ik-}+c)^3}$ (12B)
- $(\lambda_{ik}, \lambda_{ik})$: $g_{\lambda_{ik}} = \frac{2c\bar{\lambda}_{ik}}{[s\bar{\lambda}^2_{ik}+c)^2}$, $g_{\lambda_{ik}\lambda_{ik}} = \frac{2c(c-3s\bar{\lambda}^2_{ik})}{[s\bar{\lambda}^2_{ik}+c)^3}$ (12C)
- $(\lambda_{ik-}, \lambda_{ik-})$: $g_{\lambda_{ik-}} = \frac{-2rc\bar{\lambda}_{ik-}}{[s\bar{\lambda}^2_{ik-}+c)^2}$, $g_{\lambda_{ik-}\lambda_{ik-}} = \frac{-2rc(c-3s\bar{\lambda}^2_{ik-})}{[s\bar{\lambda}^2_{ik-}+c)^3}$ (12D)
- $g_{\lambda_{i1}\lambda_{i2}} = 0$ (12E)

The TS-2 approximation for the variance, $var(\hat{\lambda}'_{ijk})$, is:

$$var(\hat{\lambda}'_{ijk}) \approx f^2_{\varepsilon_{ijk}}\sigma^2_{\varepsilon_k} + f^2_{\varepsilon_{ijk-}}\sigma^2_{\varepsilon_{k-}} + f^2_{\lambda_{ik}}\sigma^2_{\lambda_{ik}} + f^2_{\lambda_{ik-}}\sigma^2_{\lambda_{ik-}} + 2f_{\lambda_{i1}\lambda_{i2}}cov(\lambda_{i1},\lambda_{i2}), \quad (13)$$

where $f_{\lambda_{i1}\lambda_{i2}}$ is given in (11), the weights f_x are

$$f_x = \frac{1}{2}g_x(1 + \frac{g}{\sqrt{g^2+\delta}}, \quad (14)$$

and the various cases for the partials, g_x, are in (12A)-(12E).

The TS-2 approximation for the covariance, $cov\left(\hat{\lambda}'_{ij1},\hat{\lambda}'_{ij2}\right)$, is complicated by the fact that it involves two (transformed) random responses: $\hat{\lambda}'_{ij1}$ and $\hat{\lambda}'_{ij2}$:

$$cov\left(\hat{\lambda}'_{ij1},\hat{\lambda}'_{ij2}\right) \approx f_{\varepsilon_{ij1}}\overleftarrow{f}_{\varepsilon_{ij1}}\sigma^2_{\varepsilon_1} + f_{\varepsilon_{ij2}}\overleftarrow{f}_{\varepsilon_{ij2}}\sigma^2_{\varepsilon_2} + f_{\lambda_{i1}}\overleftarrow{f}_{\lambda_{i1}}\sigma^2_{\lambda_{i1}} + f_{\lambda_{i2}}\overleftarrow{f}_{\lambda_{i2}}\sigma^2_{\lambda_{i2}} + (f_{\lambda_{i1}}\overleftarrow{f}_{\lambda_{i2}} + f_{\lambda_{i2}}\overleftarrow{f}_{\lambda_{i1}})\,cov(\lambda_{i1},\lambda_{i2}) \quad (15)$$

where all of the partials of the form, f_x, are given in (14). However, the term, $\overleftarrow{f}_x$, requires some explanation. Because of the symmetries of the graded transformation (6), $\hat{\lambda}'_{ijk} = f\left(\lambda_{ik}, \lambda_{ik-}, \varepsilon_{ijk}, \varepsilon_{ijk-}\right)$ and $\hat{\lambda}'_{ijk-} = f\left(\lambda_{ik-}, \lambda_{ik}, \varepsilon_{ijk-}, \varepsilon_{ijk}\right)$, i.e., $\hat{\lambda}'_{ijk}$ is $\hat{\lambda}'_{ijk-}$ but with *k* and *k-* arguments reversed. This symmetry suggests that partials on the "reverse *f*", call it $\overleftarrow{f}$, can be calculated as partials on *f* if we reverse *k* and *k-* everywhere. For example, we use 2 steps to compute $\overleftarrow{f}_{\varepsilon_{ij1}}$ in the TS-2 expression (15): (1) Find the partial, $f_{\varepsilon_{ij2}}$ and then (2) Evaluate it at the reverse (mean) argument $\left(\bar{\lambda}_{i2}, \bar{\lambda}_{i1}, 0,0\right)$. All expressions needed for f_x are given in (14). We can compute the TS-2 or STS-2 versions of *rnoise(i)'*. For STS-2

$$rnoise(i)' \approx \frac{-r\bar{\lambda}^2_{i1}\sigma^2_{\hat{\lambda}_{ij1}} - rR^4\bar{\lambda}^2_{i2}\sigma^2_{\hat{\lambda}_{ij2}} + R^2\bar{\lambda}_{i1}\bar{\lambda}_{i2}(1+r^2)cov(\lambda_{i1},\lambda_{i2})}{\sqrt{\left(\bar{\lambda}^2_{i1}\sigma^2_{\hat{\lambda}_{ij1}} + r^2R^4\bar{\lambda}^2_{i2}\sigma^2_{\hat{\lambda}_{ij2}}\right)\left(r^2\bar{\lambda}^2_{i1}\sigma^2_{\hat{\lambda}_{ij1}} + R^4\bar{\lambda}^2_{i2}\sigma^2_{\hat{\lambda}_{ij2}}\right)}} \quad (16)$$

where $R = \frac{\bar{\lambda}_{i1}^2 + c/s}{\bar{\lambda}_{i2}^2 + c/s}$ captures all the effects of *s* and *c*. Equation (16) simplifies at *r=0* to be *rnoise(i)' ≈ rnoise(i),* i.e., the transform has (approximately) no effect; this applies to TS-2 and STS-2 since the constraint is not needed.

For Case 4, i.e., the smoothed transformed data (and *rsignal~'*), exact solutions are impractical because they require conditioning on at least 6 partially-dependent random variables with integrations over a complicated region of feasibility. Now, let $\hat{v}'_{ik} = \frac{\sum_{j=1}^{N} \hat{\lambda}'_{ijk}}{N}$ and $\hat{v}'_{*k} = \frac{\sum_{i=1}^{M} \hat{v}'_{ik}}{M}$. Then, we can provide expressions for the TS-2 and STS-2 components of *rsignal~'*. That is, the expressions for $E(\hat{v}'_{ik})$, $var(\hat{v}'_{ik})$ and $cov(\hat{v}'_{i1}, \hat{v}'_{i2})$ are the corresponding versions of the untransformed responses, but in TS-2 the measurement-error variances, $\sigma^2_{\varepsilon_k}$ and $\sigma^2_{\varepsilon_{k-}}$ are divided by N and in STS-2, $\sigma^2_{\lambda_{ijk}}$ and $\sigma^2_{\lambda_{ijk-}}$ are replaced by $\sigma^2_{\hat{v}_{ik}}$ *and* $\sigma^2_{\hat{v}_{ik-}}$. If we used the classical correlation, $rsignal(i)' = \frac{cov(\hat{v}'_{i1}, \hat{v}'_{i2})}{\sqrt{var(\hat{v}'_{i1}) var(\hat{v}'_{i2})}}$, we would have all we need for TS-2 and STS-2. The STS-2 expression for *rsignal(i)'* would be (16) with $\sigma^2_{\lambda_{ijk}}$ replaced by $\hat{v}'_{ik}$ for *k=1, 2*. Moreover, for TS-2 and STS-2, we would find that when *r=0*, *rsignal(i)'≈ rsignal(i)*, i.e., that transform does not affect correlation (as for *rnoise(i)'*). However, the "pseudo-correlation",

$$rsignal{\sim}' = \frac{E\sum_{i=1}^{M}(\hat{v}'_{i1} - \hat{v}'_{*1})(\hat{v}'_{i2} - \hat{v}'_{*2})}{\sqrt{E\sum_{i=1}^{M}(\hat{v}'_{i1} - \hat{v}'_{*1})^2 E\sum_{i=1}^{M}(\hat{v}'_{i2} - \hat{v}'_{*2})^2}}, \qquad (17)$$

$$E\sum_{i=1}^{M}(\hat{v}'_{ik} - \hat{v}'_{*k})^2 = \frac{M-1}{M}\sum_{i=1}^{M}[var(\hat{v}'_{ik}) + E^2(\hat{v}'_{ik})] - \frac{1}{M}\sum_{i=1}^{M}\sum_{m \neq i}[cov(\hat{v}'_{ik}, \hat{v}'_{mk}) + E(\hat{v}'_{ik})E(\hat{v}'_{mk})], \qquad (18)$$

$$E\sum_{i=1}^{M}(\hat{v}'_{i1} - \hat{v}'_{*1})(\hat{v}'_{i2} - \hat{v}'_{*2}) = \frac{M-1}{M}\sum_{i=1}^{M}[cov(\hat{v}'_{i1}, \hat{v}'_{i2}) + E(\hat{v}'_{i1})E(\hat{v}'_{i2})]] - \frac{1}{M}\sum_{i=1}^{M}\sum_{m \neq i}[cov(\hat{v}'_{i1}, \hat{v}'_{m2}) + E(\hat{v}'_{i1})E(\hat{v}'_{m2})] \qquad (19)$$

where we usually assume $cov(\hat{v}'_{ik}, \hat{v}'_{mk})$ and $cov(\hat{v}'_{i1}, \hat{v}'_{m2})$ are neglibile for $i \neq m$.

IV. ANALYTICAL AND SIMULATION RESULTS

Before we discuss results, let us overview our simulation. Our simulation generates random measured responses ($\hat{\lambda}_{ijk}$) to various stimuli in visual neuroscience experiments. While $\hat{\lambda}_{ijk}$ are often modeled as Poisson, we assume that they are Bi-Normal with $BN\left(\bar{\lambda}_{i1}, \sigma^2_{\hat{\lambda}_{ij1}}; \bar{\lambda}_{i2}, \sigma^2_{\hat{\lambda}_{ij2}}; \rho(\hat{\lambda}_{ij1}, \hat{\lambda}_{ij2})\right)$. For each simulation sample, we generate *2xNxM* random responses. We consider various pairs of values for the mean responses ($\bar{\lambda}_{i1}, \bar{\lambda}_{i2}$), each on [25,50]. In assigning key parameter values, we prescribe response correlation to be $\rho(\lambda_{i1}, \lambda_{i2}) = 0.7$ for all stimuli, *i* and let the coefficient of variation for λ_{ik} be 5%, i.e., $var(\lambda_{ik}) = (0.05E(\lambda_{ik}))^2$. Next, we *derive* values for the (Poisson) measurement error variances, $var(\varepsilon_{ijk})$. Finally, we compute the statistics required for Cases 1-4 and contrast them to those obtained analytically. To assure the statistical validity, we generate up to ***S****=500* experiment "samples" and we correct biases, for Cases 1, 3 variance and covariance estimates, as in Sections III-B and III-C.

In Section IV-A, we provide only brief comments on Cases 1 and 2, the untransformed responses, because our analytical models are "exact". In Section IV-B, we look at simulation and T-S analytical results for the transformed responses; we focus on Case 3 statistics, $var(\hat{\lambda}'_{6j1})$ and *rnoise(6)',* because Case 4 observations do not change significantly as we vary key parameters. This similarity of empirical results is quite consistent with the striking similarity of the approximate analytical results in Section III-C.

A. *Cases 1 and 2: Untransformed Responses*

For *classical* means and covariances, the true, measured and smoothed analytical results are the same. However, the unsmoothed and smoothed *classical* variances may differ significantly because averaging reduces the variance of measured responses. The key challenge for these Cases is to make sure the simulation yields accurate estimates of the associated transformed results for Cases 3 and 4. In that regard, we note the following:

- The simulation biases for variances and covariances, are corrected as in Section III-B.
- "Pseudo variances and covariances" seem to differ only slightly from the classical ones.
- Correlation statistics, *rnoise(i)* and *rsignal~*, are difficult to estimate, may be unstable, using simulation (or experimental data) because they are ratios of other statistics.

B. *Cases 3 and 4: Transformed Responses*

Using our simulation, we studied extensively the accuracy of TS-2 and STS-2 for the moments of transformed response statistics. The transformed cases are difficult to analyze:

- The transformation, as in (6), introduces many additional parameters.
- Transformations are nonlinear, further complicated by the non-negativity constraint.
- Transformed responses are quite small, on the order of 10^{-3} to 10^{-4} for Case 4, and approaching *0* for parameter extremes, e.g., large values for *s, c*, or *r*.

In addition, variances and covariances are much more challenging than means to estimate, at parameter extremes, and correlations depend strongly on variance and covariance accuracy. We also know that STS-2 will (TS-2 may not) have accuracy problems where the non-negativity constraints are needed. We will see that, despite these difficulties, TS-2 and STS-2 are accurate and fast over important parameter ranges.

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Neuroscientists restrict *r* to be on [0,1], and often in the "neighborhood" of 0.5. However, in our analyses, we extend the domain to [0,1.5] to better understand the properties of the transforms and our models. We use the ratio *c/s* in our examples because, in our studies, we found that individual values of *s* and *c* matter only at extremes (e.g., *s=0*, *c=0,* or *r>> 0.5*). For example, the STS-2 expression for *rnoise(i)'* (16) only depends on *c/s*. We assume arbitrarily *i=6, k=1*.

1) Accuracy of Analytical Models for Variances. In Figure 1, below, we look at the accuracy of TS-2 and STS-2 (vs. simulation) of $var(\hat{\lambda}'_{6j1})$ as we vary r, c/s and $(\bar{\lambda}_{61}, \bar{\lambda}_{62})$. The rows of graphs correspond to different values of c/s and columns to ratios $\frac{\bar{\lambda}_{62}}{\bar{\lambda}_{61}}$. For each graph, the y-axis is $var(\hat{\lambda}'_{6j1})$ and the x-axis is $0 \le r \le 1.5$. Some observations:

- For these data, the analytical and simulation results match well except for STS-2 when *r>>0.5* or $\frac{\bar{\lambda}_{62}}{\bar{\lambda}_{61}} >> 1$. The analytical model "errors" are usually small in absolute value.
- The $var(\hat{\lambda}'_{6j1})$ graph is a unimodal non-negative function of *c/s*, starting at *0* when *c/s=0*, becoming positive and then approaching *0* again for large *c/s*. While not shown here, all three models do a good job of exhibiting this property.
- Because of the non-negativity constraint in (6), $var(\hat{\lambda}'_{6j1}) \rightarrow 0$ for large *r*. We see that TS-2 generally provides accurate estimates for large *r*, while STS-2 does not. However, neuroscientists see little practical application in their models for *r>>0.5*.
- TS-2 estimates of $var(\hat{\lambda}'_{6j1})$ are somewhat inaccurate when $\frac{\bar{\lambda}_{62}}{\bar{\lambda}_{61}} >> 1$ because the non-negativity constraint is needed. It would be much less important to $var(\hat{\lambda}'_{6j1})$ if $\frac{\bar{\lambda}_{61}}{\bar{\lambda}_{62}} >> 1$.

2) Accuracy and Stability of Correlation Statistics. Figure 2 (see the y-axes), below, helps us gain insights into the accuracy and stability of our *rnoise(i)'* models. Some observations:

- The analytical models are accurate (match the simulation well) if *r ≤ 0.75;* $\frac{\bar{\lambda}_{62}}{\bar{\lambda}_{61}} \le \frac{4}{3}$, i.e., ≈ 1 due to symmetries.
- The trajectory of *rnoise(6)'* vs. *r* is inherently volatile but necessarily within [-1,1]. It starts near *0* for *r=0,* decreases sharply as *r* increases and, when the non-negativity constraint "kicks in", turns up towards *0* again. TS-2 tracks the upturn pretty well, but (of course) STS-2 does not.
- The TS-2 model shows some apparent numerical instability, relative to the simulation, for large *r*. This is because, as the numerator $cov(\hat{\lambda}'_{6j1}, \hat{\lambda}'_{6j2})$, and denominator, $var(\hat{\lambda}'_{6j1})var(\hat{\lambda}'_{6j2})$, each approach *0*, estimates of *rnoise (6)'* approach 0/0 and are sensitive to the rates of convergence of the ratio components.
- Recall (Section III-C), that at *r=0*, *rnoise(i)' ≈ rnoise(i),* i.e., the transform is insensitive to *c/s* and $\frac{\bar{\lambda}_{62}}{\bar{\lambda}_{61}}$. This *c/s* insensitivity for *rnoise(6)'* extends to *r ≤ 0.75,* $\frac{\bar{\lambda}_{62}}{\bar{\lambda}_{61}} \approx 1$.

V. SUMMARY AND CONCLUSIONS

We conclude, based on our example analytical and simulation results, that TS-2 and STS-2 are accurate for a wide range of parameter values. Because the STS-2 models omit non-negativity constraints, their accuracy is best when *r≤ 0.75*; $\frac{\bar{\lambda}_{i2}}{\bar{\lambda}_{i1}} \le \frac{4}{3}$ for $var(\hat{\lambda}'_{ij1})$and $\frac{\bar{\lambda}_{i2}}{\bar{\lambda}_{i1}} \approx 1$ for correlation, *rnoise(i)'*. In addition, their simple expressions help us better understand relationships between model parameters and results. Our approximations are extremely fast, linear combinations of input parameters, with algebraic expressions for the weights. Two key conclusions for neural coding are:

- Transformations, such as normalization, can influence noise correlations, but the relationship between these two factors, *rnoise(i)* and *rnoise(i)' (*or between *rsignal' and rsignal)*, is highly sensitive to parameter choices, and hence unlikely to be robust in real neural networks.
- Opponent processing, i.e., the combining of response data from multiple neurons, has a profound influence on noise correlations.

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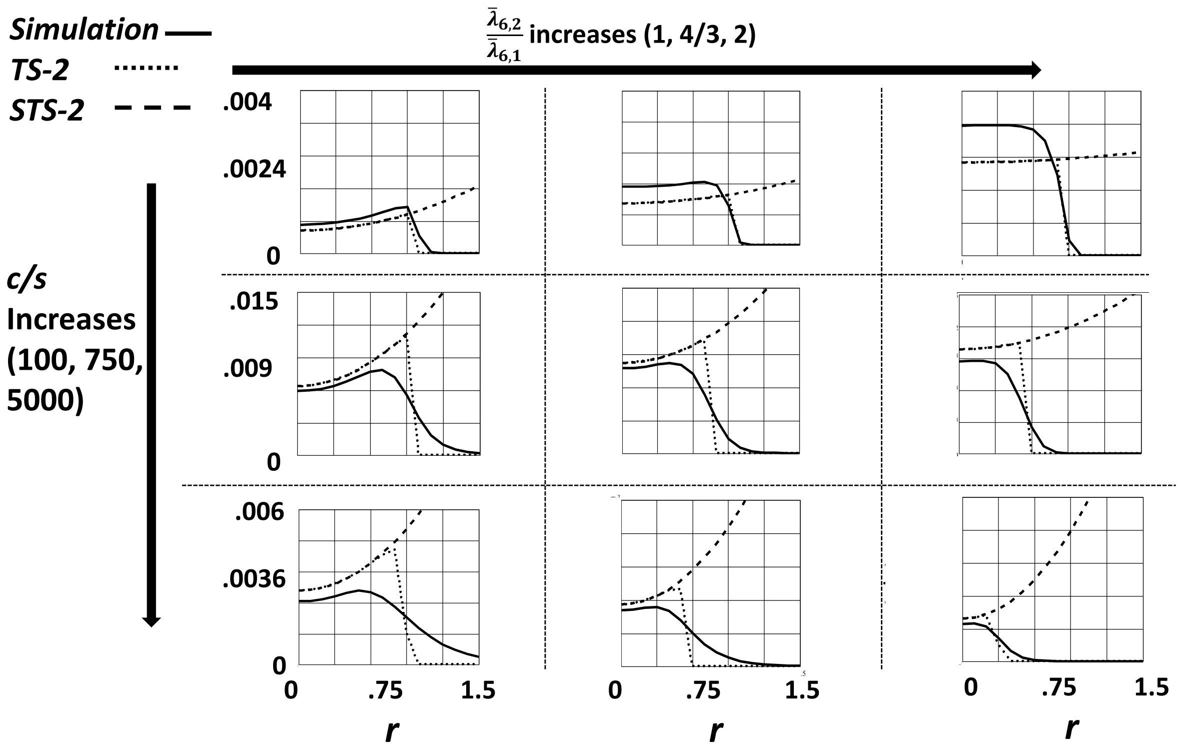

Figure 1. Transformed Variances, $var(\hat{\lambda}'_{6j1})$, vs. r

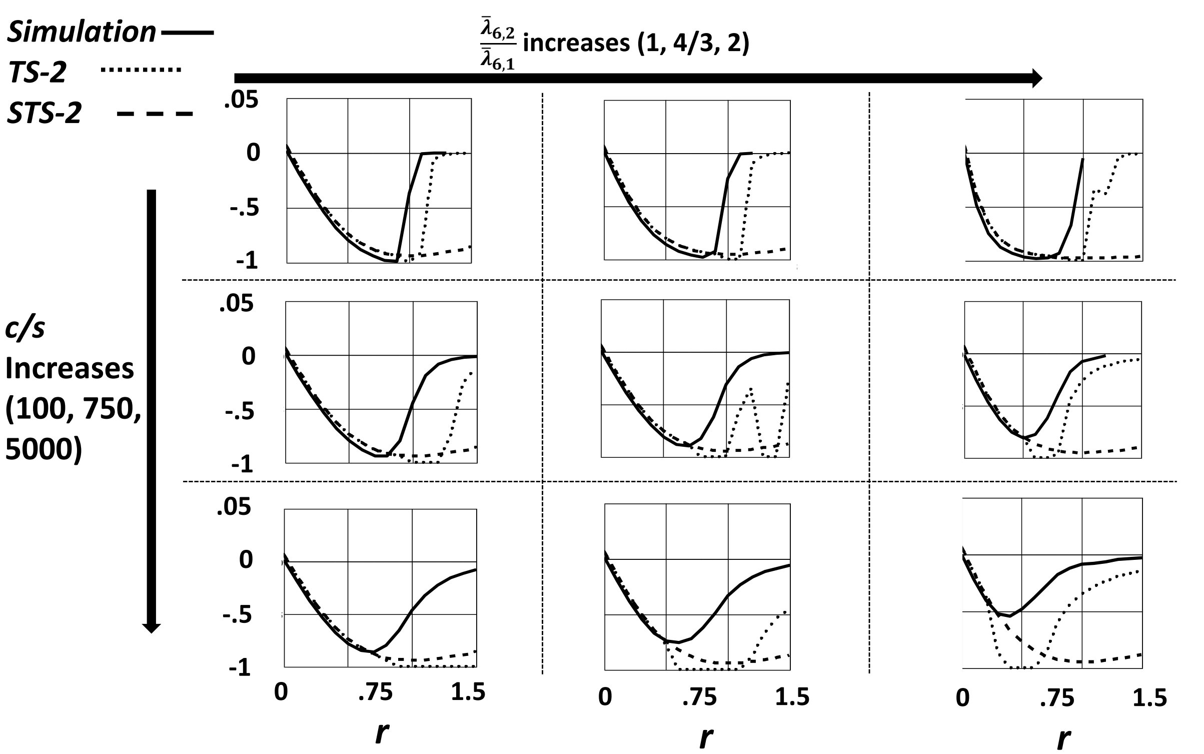

Figure 2. Correlation Statistics, *rnoise(6)'*, vs. r

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