Correlations and Neuronal Population Information

Kohn, Adam; Coen-Cagli, Ruben; Kanitscheider, Ingmar; Pouget, Alexandre

How to cite

KOHN, Adam et al. Correlations and Neuronal Population Information. In: Annual review of neuroscience, 2016, vol. 39, p. 237–256. doi: 10.1146/annurev-neuro-070815-013851

This publication URL: https://archive-ouverte.unige.ch/unige:86851
Publication DOI: 10.1146/annurev-neuro-070815-013851

Review in Advance first posted online on April 21, 2016. (Changes may still occur before final publication online and in print.)

Correlations and Neuronal Population Information

Adam Kohn,[1,2] Ruben Coen-Cagli,[3] Ingmar Kanitscheider,[3,4,5] and Alexandre Pouget[3,6,7]

[1]Dominick Purpura Department of Neuroscience, Albert Einstein College of Medicine, Bronx, New York 10461; email: adam.kohn@einstein.yu.edu

[2]Department of Ophthalmology and Visual Sciences, Albert Einstein College of Medicine, Bronx, New York 10461

[3]Department of Basic Neuroscience, University of Geneva, CH-1211 Geneva, Switzerland; email: Ruben.CoenCagli@unige.ch, alexandre.pouget@unige.ch

[4]Center of Learning and Memory, The University of Texas at Austin, Austin, Texas 78712; email: IKanitscheider@mail.clm.utexas.edu

[5]Department of Neuroscience, The University of Texas at Austin, Austin, Texas 78712

[6]Department of Brain and Cognitive Sciences, University of Rochester, Rochester, New York 14627

[7]Gatsby Computational Neuroscience Unit, University College London, W1T 4JG London, United Kingdom

Annu. Rev. Neurosci. 2016. 39:237–56

The *Annual Review of Neuroscience* is online at neuro.annualreviews.org

This article's doi: 10.1146/annurev-neuro-070815-013851

Keywords

neural coding, theoretical neuroscience, perception, Fisher information, decoding, neural variability

Abstract

Brain function involves the activity of neuronal populations. Much recent effort has been devoted to measuring the activity of neuronal populations in different parts of the brain under various experimental conditions. Population activity patterns contain rich structure, yet many studies have focused on measuring pairwise relationships between members of a larger population—termed noise correlations. Here we review recent progress in understanding how these correlations affect population information, how information should be quantified, and what mechanisms may give rise to correlations. As population coding theory has improved, it has made clear that some forms of correlation are more important for information than others. We argue that this is a critical lesson for those interested in neuronal population responses more generally: Descriptions of population responses should be motivated by and linked to well-specified function. Within this context, we offer suggestions of where current theoretical frameworks fall short.

Contents

INTRODUCTION

Technological innovation has provided us with the ability to monitor the activity of many neurons simultaneously in intact neural circuits. It is now quite common to record from a hundred neurons at a time. A major focus of the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative is to increase this capability further (Jorgenson et al. 2015).

The spiking activity of neuronal populations is coordinated, producing seemingly complex activity patterns. A rich and diverse description of these patterns already exists, including traveling waves of activity (Sato et al. 2012), rhythmic fluctuations in different frequency bands (Buzsaki 2006), complex higher-order patterns (Ohiorhenuan et al. 2010), and many others.

One form of coordination that has received considerable attention is the relationship between the firing of pairs of neurons—termed correlations. Given our ability to measure large populations, it may seem odd to distill their activity to quantification of pairwise relationships: Understanding this second-order statistical structure is unlikely to capture fully the rich patterns of neuronal population activity observed (but see Schneidman et al. 2006). However, the focus on correlations is not an inappropriate simplification. Rather, it arises because correlations have a strong impact on the information encoded by a neuronal population, particularly on the portion of information that can be extracted with simple and biologically realizable algorithms.

Our understanding of how correlations affect information has evolved considerably. We believe this progress is important for two reasons. First, it represents an achievement in its own right: We now understand much better what limits the representation of sensory and cognitive variables in neuronal populations. This is critical for understanding the neural basis of behavior, as nearly any behavior involves the activity of many neurons. Second, and perhaps equally important, this progress has shown the importance of grounding physiological measurements in quantitative theory. Correlations can be driven by many underlying processes and take many distinct forms. But theory has shown that some correlations may be more functionally relevant than others. We believe this is a critical lesson for studying population activity more generally. Rather than seeking to describe activity patterns more and more richly, progress will require understanding the relationship between activity and computation through theory.

Here we provide a brief review of how correlations affect population information and how this influence can, and cannot, be quantified. We also discuss progress in understanding how correlations arise. Because our focus is on understanding the relationship between information and correlations, we touch only briefly on the study of correlations more generally—in this sense, our work by no means attempts a complete review of the field. We conclude with thoughts about some clear shortcomings in current theoretical frameworks. We focus on populations of cortical

neurons, particularly those in visual cortex, which have been studied extensively, but the issues we review and discuss are broadly applicable.

DIFFERENT TYPES OF CORRELATIONS

Correlation is a simple statistical measure of association among variables. It is thus not surprising that the term is used to refer to distinct types of associations, or relationships, among the activities of neurons.

Correlations are sometimes used to quantify the degree to which neurons have similar functional properties. For instance, the similarity of the orientation tuning of two neurons in primary visual cortex (V1) can be quantified as the correlation between the pairs' tuning functions. Measuring these correlations—termed signal correlations—requires presenting a range of stimuli to assess functional properties, averaging responses across trials, and computing the correlation between the resultant mean responses (i.e., tuning functions).

Influential work by Barlow and others has argued that an efficient representation involves, in part, minimizing correlations between encoding units (i.e., decorrelation; Barlow 2001, Simoncelli & Olshausen 2001). These theories address how tuning functions should be arranged to reduce representational redundancy. These are thus theories of signal correlations, although the optimal arrangement is also known to depend on the properties of encoding units' response variability (Atick & Redlich 1990, Ganguli & Simoncelli 2014).

Correlations are also used to quantify the similarity in the response of a population of neurons to two different stimuli (e.g., two odors)—termed pattern correlations. Whereas signal correlations quantify the similarity between mean responses of two neurons across multiple stimuli, pattern correlations capture the similarity of activity patterns distributed across multiple neurons for two stimuli (Friedrich & Laurent 2001, Friedrich 2013).

Our focus here is on yet another type of correlation, which captures the degree to which response variability is shared between pairs of neurons. Neurons typically show substantial response variability, evident as fluctuations in the number of spikes evoked by a stimulus across multiple presentations (Tolhurst et al. 1983, Shadlen & Newsome 1998). A small portion of this variability is shared between neighboring neurons in cortex. This can be quantified with the Pearson correlation of the pairs' spike counts to repeated presentations of the same stimulus. These correlations—often termed spike count correlations (r_{sc}) or noise correlations—usually have mean values of 0.01–0.2, with their magnitude depending on a broad range of factors (Cohen & Kohn 2011). For brevity, we refer hereafter to these correlations in trial-to-trial variability simply as correlations.

CORRELATIONS AND INFORMATION: A BRIEF HISTORY

In a seminal study, Zohary and colleagues (1994) measured correlations between pairs of neurons in area MT of macaque monkeys. Their measurements were motivated by a desire to explain why monkeys' performance on a discrimination task was not considerably better than the performance afforded by the most sensitive MT neuron recorded. Although the variable responses of individual neurons limit the information they provide about the external stimulus, the responses of many neurons could be pooled or averaged to arrive at a precise estimate of the stimulus if the variability of each neuron were independent. Zohary et al. (1994) found, however, that MT response variability was correlated for neurons with similar functional properties. This shared variability cannot be averaged away, limiting the benefit of pooling signals over greater numbers of neurons. This limited benefit holds true for any positive level of correlation.

Averaging neuronal responses is conceptually simple and provides helpful intuition, but it is not always a sensible strategy for extracting information from a neuronal population. Neurons have a range of functional properties and sensitivities. Rather than weighting all neurons equally by averaging, it makes sense to weight evidence from some neurons more than others for a particular task (Pouget & Thorpe 1991, Foldiak 1993, Seung & Sompolinsky 1993, Sanger 1996, Butts & Goldman 2006, Jazayeri & Movshon 2006). There are many algorithms, or decoders, for combining signals encoded across neurons (Pouget et al. 2000). Of particular interest are linear decoders, which compute their estimates based on a simple weighted sum of the response of each neuron. These decoders are attractive because they can be learned and implemented easily in a biological circuit (Widrow & Hoff 1960, Rescorla & Wagner 1972, Pouget & Thorpe 1991, Foldiak 1993, Seung & Sompolinsky 1993, Salinas & Abbott 1994, Sanger 1996, Deneve et al. 1999, Jazayeri & Movshon 2006), where the weights assigned to each neuron might correspond to its synaptic weight in driving a downstream readout neuron.

To quantify the accuracy of a linear decoder, it is useful to consider a measure termed linear Fisher information. Intuitively, linear Fisher information measures the smallest change in the stimulus that can be discriminated reliably with an optimal linear decoder of the neuronal population response. Higher linear Fisher information means less variance in the optimal linear decoder's estimates, or better discrimination performance. Formally, linear Fisher information is defined as

$$I = \mathbf{f}'^{\top}\mathbf{Q}^{-1}\mathbf{f}',$$

where $\mathbf{f}'$ is the derivative of the tuning curve with respect to the stimulus variable of interest and $\mathbf{Q}$ is the response covariance matrix. The derivative of the tuning curve captures the signal provided by changes in mean response with changes in the stimulus; the covariance matrix captures the influence of each neuron's response variance (diagonal elements) and the variance shared with other neurons (off-diagonal elements). Note that, for brevity, we refer to the relationship between correlations and information, but information is in fact related to response covariance. The correlations reported in physiological studies—the ratio of covariance to variance (standard deviations)—confound two distinct factors that can affect information in distinct ways. Additional details on linear Fisher information and its relationship to full Fisher information are provided in the sidebar, Linear and Full Fisher Information; additional details about linear Fisher information and its relationship to fine and coarse discrimination tasks are provided in the sidebar, Linear Fisher Information for Fine and Coarse Discrimination.

Abbott & Dayan (1999) were among the first to explore the effect of correlations on Fisher information (Sompolinsky et al. 2001, Wu et al. 2001, Wilke & Eurich 2002, Averbeck et al. 2006; see also Paradiso 1988 for prescient work on populations of independent neurons). They considered a homogeneous neuronal population—one consisting of neurons with identically shaped tuning functions except that each neuron has a distinct preference. For a homogeneous population, Fisher information is reduced by correlations that are strongest between pairs of neurons with similar preferences, termed limited-range correlations. More precisely, not only is information reduced, but it saturates: It reaches a finite value even when the population size continues to grow. Numerous experimental studies have shown that correlations in cortex have a limited-range structure, including work in V1 (Kohn & Smith 2005, Smith & Kohn 2008, Ecker et al. 2010), V4 (Cohen & Maunsell 2009, Smith & Sommer 2013), and MT (Zohary et al. 1994, Bair et al. 2001, Huang & Lisberger 2009, Solomon et al. 2014) of nonhuman primates; V1 of cats (Martin & Schroder 2013); visual cortex of rodents (Denman & Contreras 2014); and many others.

Why do limited-range correlations make information saturate in populations of homogeneously tuned neurons? Consider a homogeneous population with Gaussian tuning functions

LINEAR AND FULL FISHER INFORMATION

Linear Fisher information places a bound on the variance of the estimates of any unbiased linear decoder, which must be equal to or larger than the inverse of the Fisher information (Paradiso 1988, Seung & Sompolinsky 1993, Abbott & Dayan 1999). Linear Fisher information is a component of the full Fisher information. The full Fisher information can be substantially larger than the linear Fisher information for some response distributions. However, extracting this additional information requires more sophisticated, nonlinear decoding (e.g., Shamir & Sompolinsky 2004), which may be more difficult to implement or learn in biological circuits. Furthermore, linear Fisher information is equivalent to the full Fisher information for any response distribution of the exponential family with linear sufficient statistics (Beck et al. 2011). Evidence suggests that V1 responses to stimulus orientation (Graf et al. 2011, Berens et al. 2012) and medial superior temporal area (MSTd) responses to heading direction (Fetsch et al. 2011) fall under this description, and there is no evidence that responses in other sensory areas do not. Thus, linear Fisher information is a reasonable and useful way to measure population information.

(**Figure 1*a***). A stimulus presentation will evoke a population response, which is also Gaussian, when the neurons are arranged by their preferred stimulus (**Figure 1*c***). Because neurons' responses are variable, the population response will be a noisy one. Now consider the effect of making all neurons equally correlated, regardless of preference (uniform correlations; **Figure 1*b***). This will cause the population response to fluctuate up and down on each trial without altering its shape or position (**Figure 1*c***, *red* compared to *blue*). Because the estimate of the stimulus depends on the shape and position of the population hill of activity rather than its magnitude (i.e., comparing the relative responses of different neurons), these fluctuations have little effect on a decoder's estimate. Therefore, the variance of the estimate will continue to decrease—and information to increase—as the population size grows (**Figure 1*f***, *black line*). Limited-range correlations (**Figure 1*d***), by

LINEAR FISHER INFORMATION FOR FINE AND COARSE DISCRIMINATION

In a typical discrimination task, the subject is asked to distinguish two similar stimuli $s^+ = s + ds$ and $s^- = s - ds$. Given neuronal population responses, one can construct a linear estimator of the stimulus that is unbiased for the two presented stimuli, a locally optimal linear estimator (LOLE). Given a neuronal response pattern $\mathbf{r}$, the LOLE is given by

$$\hat{s}_{\mathbf{w}}(\mathbf{r}) = s + \mathbf{w}^T \cdot (\mathbf{r} - \frac{\mathbf{f}(s^+) + \mathbf{f}(s^-)}{2}); \quad \mathbf{w} = \frac{\bar{\mathbf{Q}}^{-1}\mathbf{f}'}{\mathbf{f}'^T \bar{\mathbf{Q}}^{-1}\mathbf{f}'},$$

where $\hat{s}_{\mathbf{w}}$ is the estimate of the stimulus and $\mathbf{f}' = (\mathbf{f}(s^+) - \mathbf{f}(s^-))/(2ds)$ and $\bar{\mathbf{Q}} = (\mathbf{Q}(s^+) + \mathbf{Q}(s^-))/2$ are the difference quotient of the tuning curves and the average covariance matrix, respectively. Linear Fisher information is defined as the inverse of the average variance of the LOLE for the true presented stimuli (Series et al. 2004),

$$I = \frac{2}{\mathrm{Var}(\hat{s}_{\mathbf{w}}(\mathbf{r}) \mid s^+) + \mathrm{Var}(\hat{s}_{\mathbf{w}}(\mathbf{r}) \mid s^-)} = \mathbf{f}'\bar{\mathbf{Q}}^{-1}\mathbf{f}'.$$

Note that one can always construct the LOLE explicitly. As a consequence, linear Fisher information is always attainable, unlike the full, nonlinear Fisher information.

It is common to distinguish fine and coarse discrimination tasks depending on whether ds is small or large. The definition of the LOLE and the expression for linear Fisher information above does not assume that ds is small; it is valid for both fine and coarse discrimination.

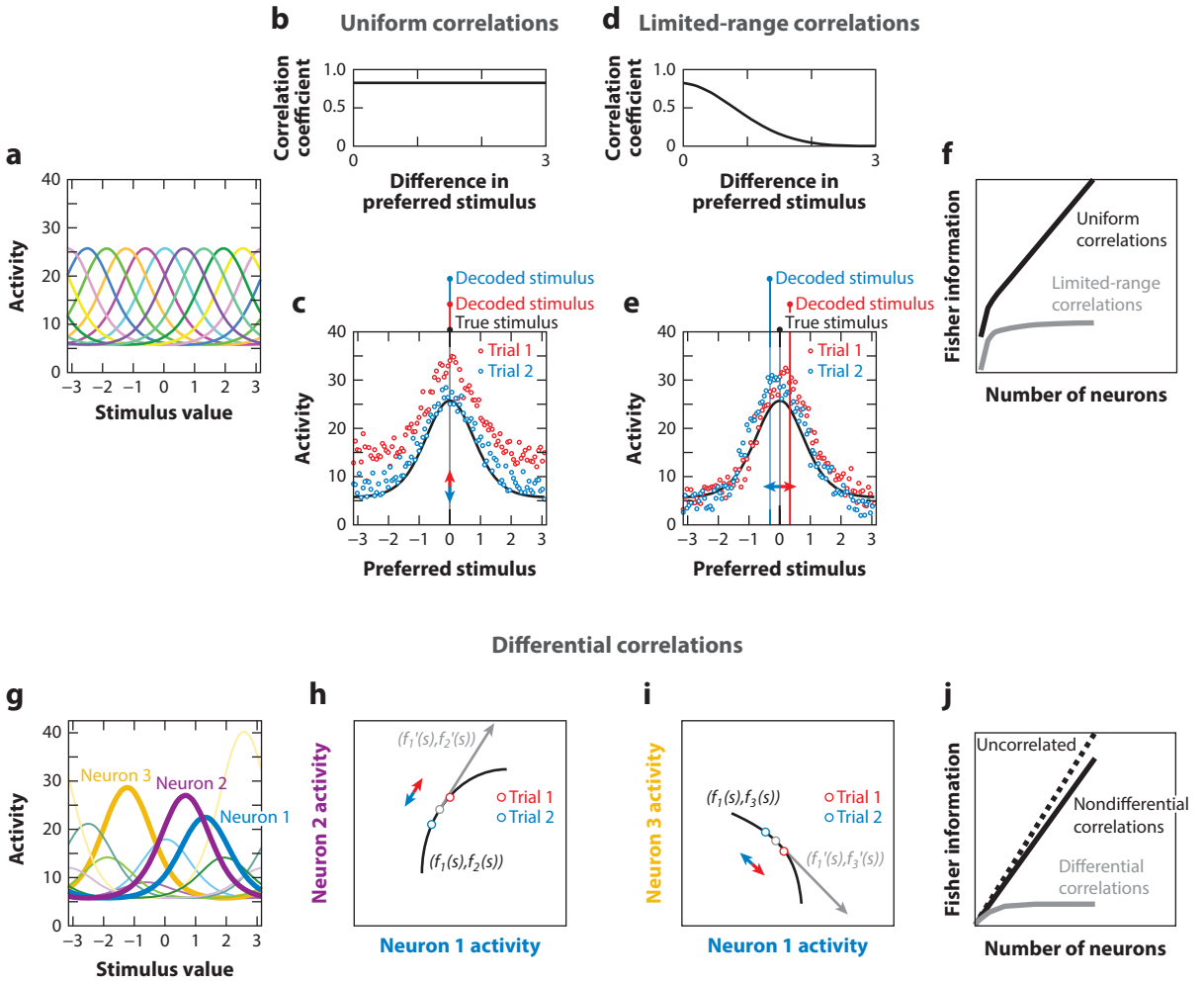

Figure 1

How different forms of correlations affect information. (*a*) A homogeneous neuronal population, having identical tuning except for the preferred stimulus value (arbitrary units). (*b*) Uniform correlation structure, in which all neurons are equally correlated regardless of preference. (*c*) Population activity in two individual trials (*red* and *blue circles*) in response to a stimulus value of 0. Neurons are sorted by their preferred stimulus value (abscissa). The trial-averaged response is shown by the black line. Additive noise that is positively correlated across all units produces vertical shifts of the population hill of activity. In a large population, such fluctuations can be averaged out entirely by using the optimal decoder; therefore, in each trial, the decoded stimulus value is identical to the true value. (*d*) Limited-range correlation structure, in which neurons with similar preferences are more strongly correlated. Note that correlation magnitude is unrealistically large to visualize clearly its effect on population activity. (*e*) Limited-range correlations distort the population activity profile in a way that cannot be averaged out, leading to variable estimates of the stimulus value. Conventions as in panel *c*. (*f*) Fisher information as a function of population size for uniform (*black*) and limited-range (*gray*) correlations. (*g*) A neuronal population with heterogeneous tuning. (*h*) The activity of two neurons, plotted against each other. The black line indicates the average responses evoked in these neurons by a range of stimuli, defined by their tuning; the gray arrow indicates the derivative of this tuning. Differential correlations correspond to variability that changes the neural responses across trials (*red* and *blue circles*) along the direction parallel to the tuning curve derivative (*red* and *blue arrows*). For these two neurons, the derivatives have the same sign; hence, the differential correlations are positive. (*i*) Same as panel *h*, but for neurons that have derivatives with opposite signs; hence, the differential correlations are negative. (*j*) A graphical representation of the fact that linear Fisher information increases linearly with the number of neurons in an independent population (*dashed line*) and with some types of nondifferential correlations (*black*, *continuous line*), but with different slopes. Information saturates to a finite value with differential correlations (*gray line*).

contrast, will cause subsets of neighboring neurons to fluctuate together. This is because a particularly weak or strong response of a neuron on a given trial will be shared by neurons with similar preferences but much less so by neurons with different preferences. These local, shared fluctuations distort the population response on each trial. For instance, for the two trials shown in **Figure 1*e***, there is enhanced responsivity in subsets of neurons slightly offset from those that prefer the presented stimulus (preferred stimulus of 0). These distortions cause the decoder's estimates to deviate from the true stimulus and thus will cause information to saturate (**Figure 1*f***, *gray*).

Although linear Fisher information saturates with limited-range correlations in homogenous populations, this is not always the case in populations with heterogeneous tuning (Shamir & Sompolinsky 2006, Ecker et al. 2011)—that is, if the tuning of neurons differs in amplitude or shape (**Figure 1*g***), as it does in most brain areas. In heterogeneous populations with limited-range correlations, information can grow with population size, much as it does in populations of independent neurons. If limited-range correlations do not make information saturate in populations of heterogeneously tuned neurons, then what—if anything—does?

Moreno-Bote et al. (2014) recently showed the answer is beguilingly simple. It can be appreciated by reexamining the equation for linear Fisher information provided above: The aspect of response covariance that influences information is that which is related to the derivative of the tuning functions (specifically, proportional to the product of the derivatives of the tuning). Correlations with this structure—termed differential correlations—cause information to saturate. This is true regardless of the shape of the tuning functions. Differential correlations also cause information to saturate in homogeneous populations; it is simply that in these populations, limited-range correlations contain differential correlations.

To understand why differential correlations make information saturate, consider an observer performing the perceptual task of estimating stimulus orientation. If in each trial we perturb the stimulus slightly by a small rotation, we will hamper the subject's performance artificially. The subject's estimates will be less accurate because our stimulus manipulation will alter the responses of orientation-selective neurons in a way predicted by the derivative of the tuning curve (by definition, the derivative indicates how responses change for small perturbations). Now consider the more typical scenario in which the stimulus is fixed but the neural representation varies across repeated trials of the task. The variability that will limit performance is that which causes fluctuations in the same manner as variations in the external signal. This is precisely the definition of differential correlations—they indicate response cofluctuations that cause population responses to fluctuate in the same manner as the fluctuations that would be caused by perturbing the signal itself (**Figure 1*b*,*i***).

Critically, although differential correlations cause information to saturate, their contribution to overall correlations may be negligible (Moreno-Bote et al. 2014, Kanitscheider et al. 2015b). Thus, measuring the relationship between correlations and the tuning functions' derivative directly may not allow one to assess the presence or influence of differential correlations accurately. The next best way to test for their presence would be to test whether information saturates as population size increases. This would perhaps require recording from thousands of neurons simultaneously (Kanitscheider et al. 2015b), which may soon be possible. Yet another possibility is to examine the relationship between an animal's behavioral report and the fluctuations of a single neuron across trials. Using this approach, Pitkow et al. (2015) found evidence recently that vestibular areas use a code containing differential correlations.

Although differential correlations cause information to saturate (Moreno-Bote et al. 2014), the total information in a sensory population can also be affected by nondifferential correlations (those that are not related to the tuning curve derivative). Consider a population of independent neurons. Information in this population is proportional to its size—adding neurons causes information

to grow, without bound (**Figure 1*j***, *dotted line*). This description also applies to heterogeneous populations with some kinds of nondifferential correlations (e.g., uniform additive noise; Abbott & Dayan 1999), but information grows more slowly with population size (**Figure 1*j***, *black line*). If information grows five times more slowly, for instance, the correlated population will contain only 20% of the information of an equivalently sized independent population. Thus, nondifferential correlations can lower information significantly. However, differential correlations have a much bigger effect because information saturation means that the percentage of information compared to an independent code goes to zero as population size grows (**Figure 1*j***, *gray line*). As discussed below, nondifferential correlations can also affect strongly information in small populations and the information at saturation in large populations through their interactions with differential correlations.

In summary, the study of population information is marked by an evolution in our understanding of which correlations matter. The work of Zohary and colleagues (1994) posited that neuronal responses should be pooled to arrive at an accurate estimate of population firing rate; in this scenario, the existence of any correlations within the pool are detrimental. The introduction of Fisher information and its application to homogeneous populations led to the suggestion that limited-range correlations make information saturate. Finally, the incorporation of heterogeneous tuning led to the realization that only differential correlations cause information saturation. Thus, as theory has improved, it has fundamentally altered our understanding of which forms of correlation are functionally important for limiting information.

ESTIMATING LINEAR FISHER INFORMATION

Linear Fisher information is a central quantity for understanding how correlations influence population information. Computing linear Fisher information is thus critical for understanding whether the information provided by a neuronal population is sufficient to underlie a particular function or behavior. We therefore briefly review several approaches to estimating information and highlight pitfalls to be avoided.

The form of linear Fisher information suggests that calculating it directly from measured population responses should be straightforward. It requires estimating just two quantities: the tuning function (and then taking its derivative with respect to the stimulus variable of interest) and the response covariance matrix (and then inverting it). Unfortunately, linear Fisher information calculated this way is highly inaccurate. Although estimates of tuning function derivatives and covariance matrices based on finite data are unbiased, the nonlinear transformations involved in computing linear Fisher information result in a substantial overestimation of information. Fortunately, this bias can be corrected for analytically (Kanitscheider et al. 2015a), allowing for fast and accurate direct estimation of linear Fisher information from limited experimental data, as long as the number of trials exceeds the number of recorded neurons (**Figure 2*a***).

A conservative alternative to computing linear Fisher information directly is to evaluate the performance of a linear decoder trained on the data (Series et al. 2004, Moreno-Bote et al. 2014). Because a model fit to finite data will always fit noise (overfitting), it is critical to assess performance through cross-validation—leaving out a fraction of trials from the training set and evaluating performance on these. The cross-validated performance of the decoder will provide a lower bound on the true information (**Figure 2*b***). Several studies have used this approach to quantify the effect of correlations on information in neuronal populations (e.g., Graf et al. 2011, Berens et al. 2012, Jeanne et al. 2013, Adibi et al. 2014, McDonald et al. 2014). In fact, cross-validated decoding and direct estimation provide complementary ways to quantify linear Fisher information. Direct estimation with current techniques (such as the one described in the previous paragraph) is not

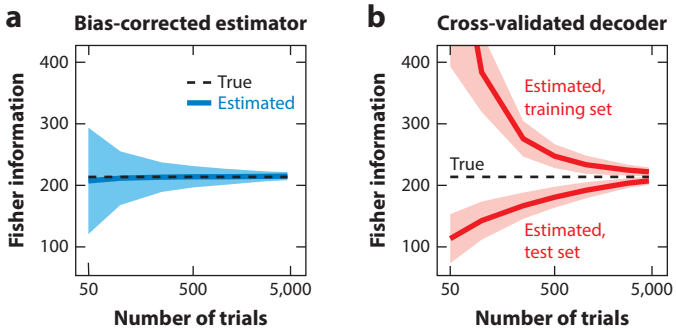

Figure 2

Estimating Fisher information from population recordings. Two estimators of Fisher information are shown that accurately capture the information present in a neuronal population. Simulations are based on 50 neurons and 200 experiments; each experiment involves a different set of parameters for the filters representing each neuron. (*a*) The direct estimator with analytical bias correction (*blue line*) provides an unbiased estimate of the true information (*dotted line*). Shaded areas represent ± 1 standard deviation of the estimate. (*b*) The performance of a trained decoder on left-out data (test set) provides a lower bound on the true information and approaches the true information when there are a sufficient number of trials. Both panels adapted with permission from Kanitscheider et al. 2015a.

feasible when there are fewer trials than neurons available, and it can underestimate information in small and uninformative populations; in these regimes, decoding is the best option. Conversely, in large and informative populations, decoding can underestimate information significantly, whereas the direct method is extremely accurate (Kanitscheider et al. 2015a).

Importantly, linear Fisher information in neural data cannot be estimated accurately through simulation. Numerous studies have measured correlations in cortex and then used parametric approximations to the observed structure to estimate information either analytically or by decoding synthesized responses (e.g., reporting that correlations have roughly a limited-range structure and then creating a covariance matrix with smoothly varying values; Gutnisky & Dragoi 2008, Smith & Kohn 2008, Ecker et al. 2010). This approach is prone to profound errors. As discussed above, the differential correlations that limit information may be tiny. If one captures only general trends in correlations through simulation, the impact of differential correlations can be lost easily, and one could conclude erroneously that the population contains much more information than it truly does (**Figure 3*a***). To avoid these problems, it is critical to estimate information using the measured responses of a simultaneously recorded population. Likewise, linear Fisher information cannot be assessed accurately with suboptimal decoders. For instance, it is possible to design a neural code in which information grows with the number of neurons but for which the information estimated by a factorized decoder saturates (**Figure 3*b***). A factorized decoder is a suboptimal decoder whose weights depend only on individual neuronal response statistics, ignoring correlations. Factorized decoders, and other suboptimal decoders, can lead to the erroneous conclusion that a population contains much less information than it truly does.

A closely related point is that one should not draw general conclusions about the impact of correlations by quantifying their effect in small neuronal populations (i.e., populations that can be recorded with current technology). The impact of correlations is typically quantified by comparing the information in the recorded, or simulated, data to that obtained after removing correlations (namely, setting the off-diagonal entries of the covariance to zero; this is called shuffled information). The relation between the two can change drastically between small and large populations. For instance, consider a code that contains differential correlations. In small populations, one

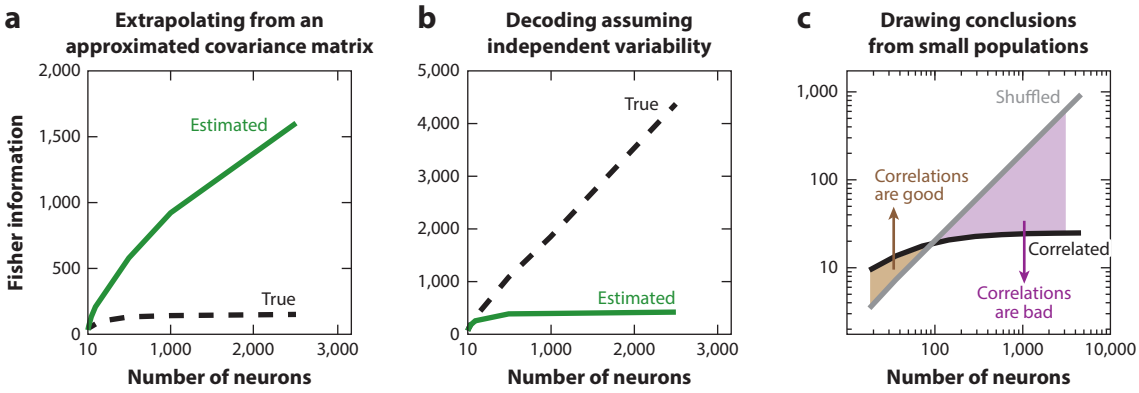

Figure 3

Common errors in estimating information. (*a*) Information in neural data can be severely misestimated when based on simulated data that approximate measured responses. Consider a synthetic population with differential correlations. For each population size N (abscissa), the true information is computed from the full population (*dashed line*) and shows clear saturation for large populations. The information estimated using an approximation to the true covariance matrix (*green line*) shows no saturation, yielding estimates that vastly exceed the true information. The estimated covariance matrix is constructed as in Moreno-Bote et al. (2014), figure 7a. Briefly, half the entries in the matrix are set to the measured value; the remaining entries are filled in by resampling the measured coefficients and enforcing that the resulting matrix is a covariance and that it has the same limited-range structure as the original data. (*b*) Suboptimal decoding can severely underestimate the true information in the population. Consider a heterogeneous population without differential correlations (model of Ecker et al. 2011). The true information grows with population size (*dashed line*); the information estimated by a suboptimal, factorized decoder (*green line*) saturates, underestimating the true information. The factorized decoder is the correlation-blind decoder of Pitkow et al. (2015). (*c*) Conclusions about the importance of correlations based on small populations do not always apply to larger populations. Consider a synthetic population with homogeneous tuning and multiplicative global fluctuations (model and parameters of Lin et al. 2015, figure 8E, with a coefficient of variation of 0.4), plus a small amount of differential correlations. For each population size (abscissa), the true information (*black line*) is computed from the true tuning and covariance matrix; the shuffled information (*gray line*) is computed after removing correlations (i.e., setting the off-diagonal entries of the covariance matrix to zero). For populations of tens of neurons, removing correlations reduces information, suggesting that correlations are helpful (*brown shaded area*). For larger population sizes, the true information saturates while the shuffled information grows linearly, showing correlations are harmful (*purple shaded area*). Thus, the conclusion that correlations increase information does not apply when considering populations that are likely to underlie function.

could find a small difference between information and shuffled information and conclude that correlations have little effect on information. However, as population size increases, the shuffled information will grow without bound while the true information will saturate owing to differential correlations, showing that these correlations have an enormous effect on information. Even worse, in some cases, one can reach opposite conclusions about how correlations affect information when analyzing small rather than large populations. For instance, Lin et al. (2015) considered a code in which correlations are beneficial rather than detrimental for small populations. However, in their code, correlations reduce information when a larger population is considered (**Figure 3*c***).

There is thus an unfortunate paradox: Information can be evaluated only by measuring it in a recorded population (either by decoding or by direct estimation), but the effect of correlations on these populations may be different from their effect on larger, more functionally relevant population sizes. Clearly, we need a better understanding of the relevant population size for a given behavior or computation, measurements from larger populations, and theoretical developments that allow us to draw correct inferences from the data we can record. For the time being, it remains very much unclear whether documented changes in correlations, such as those that occur with behavioral or stimulus manipulations, have a meaningful effect on population information.

SOURCES OF CORRELATIONS

So far we have discussed which correlations affect information without discussing how they arise. We now consider the possible sources of correlations, beginning with differential correlations because these cause information to saturate. We then consider other sources and how the correlations they generate affect information.

There are at least two potential sources of differential correlations. The first source is representational expansion: Fewer neurons exist in sensory organs than in downstream structures. For instance, in the visual system, there are considerably more V1 neurons than retinal ganglion cells or cells in the lateral geniculate nucleus. This expansion implies that the information available in the retina is small compared to the coding capacity downstream (Kanitscheider et al. 2015b). Because the information in V1 cannot exceed that provided by the retina, information in V1 cannot be proportional to the number of cortical neurons; information must saturate, implying the existence of differential correlations. The second source of differential correlations is suboptimal computation. Imagine that a variable is encoded by many independent neurons but that only one neuron projects downstream—an extreme form of suboptimal computation. Clearly, information downstream would not grow with the number of neurons there but would instead saturate to a finite value corresponding to, at most, the information conveyed by the sole input neuron. This implies that the downstream network contains differential correlations that arise from suboptimal read out. Although this example is contrived, our point is general: Suboptimal computation always reduces information (in fact, this is true by definition). And because many complex computations in the brain are suboptimal (Beck et al. 2012a), suboptimal computation is likely a major source of differential correlations.

What sources contribute to correlations more generally? An obvious and oft-cited source is shared or common input (Shadlen & Newsome 1998, Kanitscheider et al. 2015b). However, the relationship between shared inputs and correlations is not straightforward: Shared inputs do not necessarily generate strong correlations. For instance, in randomly connected networks of excitatory and inhibitory neurons (balanced networks) (van Vreeswijk & Sompolinsky 1996), fluctuations in excitatory drive are tracked rapidly by fluctuations in the activity of inhibitory neurons (Renart et al. 2010). When two neurons receive correlated excitatory drive, correlated inhibitory signals (i.e., inhibitory inputs that are correlated with each other and with the excitatory pool) largely cancel their impact on postsynaptic responses (see also Salinas & Sejnowski 2000, Graupner & Reyes 2013). This mechanistic insight can explain why correlations in cortex—a highly recurrent network in which nearby neurons likely receive massive shared input—can be weak. Indeed, this architecture has been cited as a basis for the decorrelated or asynchronous cortical state (Ecker et al. 2010, Renart et al. 2010, Tan et al. 2014, but see also Bujan et al. 2015).

Notably, however, decorrelation via a balance of excitation and inhibition cannot always remove all correlations. For a network that receives limited information (i.e., less information than would be available from a population of N independent neurons), full decorrelation would make information grow linearly with network size and thus exceed the information in the inputs. This would violate the data-processing inequality, which states that processing a signal cannot increase its information. In Renart et al. (2010), correlations do disappear altogether for large networks, but this is because the input is composed of N independent neurons, in which case the data-processing inequality is not violated. The input information grows linearly with the population size, and the full decorrelation achieved by the recurrent network (in the limit of an infinitely large population) amounts to preserving all the input information.

Although the asynchronous activity produced by balanced networks provides an important insight, these models clearly do not represent connectivity in cortical networks accurately. In cortex,

connectivity is not random but clustered: Neurons receive preferential inputs from other neurons with similar functional properties (Bosking et al. 1997, Cossell et al. 2015), and connections are much stronger between some neurons than between others (Song et al. 2005, Yoshimura et al. 2005). If the assumption of random connectivity is relaxed, quite different network dynamics are revealed. For instance, in networks with clustered connections, the firing of tightly interconnected neurons waxes and wanes together (Rasch et al. 2011, Litwin-Kumar & Doiron 2012), producing strong correlations within a local pool. Some empirical evidence suggests that correlations are stronger in networks with clustered connectivity than in networks with more homogeneous architecture (Hansen et al. 2012, Smith et al. 2013, Calabrese & Woolley 2015). Strengthening the coupling between randomly connected neurons can also result in transitions from the asynchronous state to complex network activity with strong cofluctuations (Ostojic 2014).

The preceding models emphasize the role of local connectivity patterns in generating correlations. A substantial portion of correlations may also be explained by global fluctuations in which the firing of many neurons increases or decreases together on each trial (Ecker et al. 2014, Goris et al. 2014, Pachitariu et al. 2015, Schölvinck et al. 2015). The widespread cofluctuations of cortical activity were first observed using voltage-sensitive dye imaging of macaque V1, which revealed spatially extensive regions of coherent hyper- and depolarization (Arieli et al. 1996). Building on this observation, more recent work has attempted to explain correlations as arising from a single, common cofluctuation in either an additive (Ecker et al. 2014) or multiplicative (Schölvinck et al. 2015) manner. Others have argued that the shared fluctuations involve more local shared gain factors (Goris et al. 2014) or several distinct factors distributed across the population (Yu et al. 2011, Rabinowitz et al. 2015).

The source of global fluctuations is not clear. One possibility is that they are driven by top-down or feedback inputs from higher cortex. Consistent with this possibility, several studies have shown that correlations are not hardwired by network architecture but are highly sensitive to behavioral context and brain state. For instance, the correlations between pairs of MT neurons change with task instructions: Correlations are stronger when a task requires the animal to combine a pair's signals than when a task requires the two neurons to contribute signals to distinct outcomes (Cohen & Newsome 2008; see also Roelfsema et al. 2004, Ramalingam et al. 2013 for related results in V1). Similarly, the allocation of attention can reduce correlations strongly (Cohen & Maunsell 2009, Mitchell et al. 2009, Harris & Thiele 2011, Herrero et al. 2013) but in other contexts may increase correlations (Ruff & Cohen 2014). Recent models have also shown how top-down signals from decision areas that integrate sensory evidence could inject correlations into the sensory representation (Haefner et al. 2014, Wimmer et al. 2015).

Although global fluctuations may contribute strongly to correlation magnitude, theory makes clear that this contribution is not equivalent to having an important role in limiting information. Two recent studies have reported that information is affected by global fluctuations, based on simulating (Lin et al. 2015) or analyzing (Pachitariu et al. 2015, Arandia-Romero 2016; using Shannon information) small ensembles. However, in large populations, only differential correlations can make information saturate. Global fluctuations do not create correlations of this type for most variables, except perhaps for variables such as visual contrast, which modulate the firing of most neurons in the same direction, as global fluctuations do. Although global fluctuations cannot make information saturate, multiplicative global fluctuations can lower the value at which information saturates if a population contains differential correlations (Kanitscheider et al. 2015b). This could allow top-down signals such as attention to increase information by reducing global fluctuations (Rabinowitz et al. 2015); of course, information could not increase past the saturation imposed by differential correlations. Another possibility is that top-down signals do not induce truly global fluctuations but instead modulate specific subsets of neurons (e.g., as in feature-based attention).

In this case, top-down signals may introduce differential correlations (Ecker et al. 2015). Of course, if global fluctuations are driven by top-down inputs, it is also possible that downstream decoding circuits are aware that these signals have been injected. This would allow these circuits to negate entirely any influence of the injected signals on population coding accuracy.

In summary, numerous mechanisms determine the strength and properties of correlations (see Doiron et al. 2016 for review). These include feedforward, local, or recurrent connections, as well as top-down signals. Importantly, there may be a strong dissociation between the contribution of these mechanisms to the magnitude of correlations and their effect on information.

OTHER INTEREST IN CORRELATIONS

Our focus has been on progress in understanding how correlations limit population information. This progress has shown that just quantifying correlations, without considering their exact pattern, provides little insight into population information. However, measuring correlations may be useful for understanding other aspects of brain function and organization.

First, correlations appear exquisitely sensitive to cognitive and behavioral factors (Kohn et al. 2009). They are reduced strongly by the allocation of attention (Cohen & Maunsell 2009, Mitchell et al. 2009, Herrero et al. 2013) and arousal (Poulet & Petersen 2008), even when the effect of these inputs on single-neuron firing rates is difficult to detect. Correlations are also affected strongly by adaptation (Gutnisky & Dragoi 2008, Adibi et al. 2013) and learning (Komiyama et al. 2010, Gu et al. 2011, Jeanne et al. 2013). Thus, correlations may be a sensitive indicator of brain state and a useful metric for quantifying the efficacy of behavioral manipulations (e.g., the level of arousal). However, it must be understood that these changes in mean correlations do not necessarily indicate that population information has been altered (Series et al. 2004, Bejjanki et al. 2011, Gu et al. 2011).

Second, correlations can be used to infer functional connectivity from measurements of spiking activity (Stevenson et al. 2008). Such inferences were first based on measuring the correlation in spike timing of neuronal pairs (Moore et al. 1970), a form of correlation that is mathematically related to the count correlations that we have emphasized (Bair et al. 2001). Pairwise timing correlations have been used to infer connectivity between the thalamus and cortex (Reid & Alonso 1995) and between stages of the temporal visual processing pathway (Hirabayashi et al. 2013). Detailed anatomical measurements have shown that correlation magnitude can be indicative of the interconnectedness of neurons (Gerhard et al. 2013, Cossell et al. 2015, Okun et al. 2015).

However, the relationship between correlations and network architecture is complex. Modeling work has highlighted some of the difficulties of using correlations to infer connectivity (Ginzburg & Sompolinsky 1994, Ostojic et al. 2009). For instance, weak or absent correlations do not indicate a lack of shared inputs (Renart et al. 2010), as discussed previously. Similarly, a timing relationship between two spike trains does not indicate an anatomical connection between the pair of neurons (Yu & Ferster 2013). New analytical approaches are under development to fit full population responses, allowing more accurate inferences about connectivity (Okatan et al. 2005, Pillow et al. 2008, Gerwinn et al. 2010, Masud & Borisyuk 2011). Ultimately, the use of spiking correlations—or of response dependencies, more generally—to infer connectivity may have the greatest success in systems for which there is already substantial anatomical knowledge (e.g., paired with connectomics), for which one can sample from most of the constituent elements (Pillow et al. 2008), or for which computational models make predictions about compelling patterns of correlations (Baker & Bair 2012).

Third, understanding correlations among neurons is critically important for understanding the relationship between each neuron's activity and behavioral decisions (Nienborg et al. 2012). In

recent work, Haefner and colleagues (2013) derived the relationship between a single neuron's response fluctuations and a perceptual decision (often termed choice probability), assuming a linear readout of sensory population activity (see also Pitkow et al. 2015). When large neuronal populations contribute to behavior, the weight assigned to each neuron by the readout contributes negligibly to this relationship. Instead, the relationship is dominated by the correlation between the neuron's fluctuations and the rest of the relevant pool (and the weights assigned to the neurons in that pool). Thus, understanding the structure of correlations within a population is critical for interpreting how each individual neuron contributes to a behavioral choice and how neural representations are read out.

Fourth, correlations can provide a diagnostic signature of network organization and the properties of a neural representation. For instance, just as reproducing individual neuronal response statistics places strong constraints on network models (van Vreeswijk & Sompolinsky 1996, Shadlen & Newsome 1998, Vogels & Abbott 2005, Vogels et al. 2005), capturing the magnitude and pattern of correlations under different stimulus and behavioral regimes may provide important clues about network architecture. A second, less mechanistic example is the suggestion that cortical populations represent not only point estimates of a quantity of interest but also the uncertainty associated with such estimates (Ma et al. 2006). Different proposals exist for how such probabilistic representations can be achieved, and these may create different patterns of correlations (see Pouget et al. 2013 for a review). A final example is the proposal that early cortical processing relies on probabilistic generative models of the natural sensory environment (Barlow 2001, Dayan & Abbott 2001, Simoncelli & Olshausen 2001, Fiser et al. 2010, Berkes et al. 2011). Patterns of correlations may be related to dependencies among the variables represented in such models.

SHORTCOMINGS

Given what we have learned about correlations, what are the obvious shortcomings in our current understanding? Arguably, the most pressing issues are theoretical. Much theory has been devoted to understanding how correlations affect the ability of linear decoders to estimate the value of a one-dimensional variable, such as stimulus orientation. This is an important question. It involves a clearly defined computation; performance is also easily quantified and can be related to a broad perceptual literature involving the estimation of a sensory quantity or the discrimination between stimuli. By understanding the factors that limit the sensory representation, we gain important insight into the neural constraints on perceptual performance.

However, estimating a one-dimensional variable is a gross simplification of computation in the brain. Visual processing, for example, involves a hierarchical sequence of computations, some nonlinear, with robust top-down control. Although we have some understanding of how the properties of downstream circuitry influence information loss in feedforward and simple recurrent networks (Beck et al. 2011, Renart & van Rossum 2012), we have a poor understanding of how the computations involved in sensory processing are affected by correlations. Similarly, understanding the role of correlations in higher cognitive functions—for example, classifying stimuli into categories such as aversive versus appetitive—may require a different mathematical treatment (Da Silveira & Berry 2014).

We note that there is, in fact, a striking gap in theoretical and computational neuroscience: One community focuses on the computations that build sensory representations or underlie cognitive function, neglecting variability and correlations; another focuses on variability and correlations, but in the context of limited and simple computation (but see Beck et al. 2012b, Grabska-Barwińska et al. 2014, Hennequin et al. 2014). Recent work has shown the problems that can arise because of this gulf. An oft-cited strategy for untangling sensory information (Friedrich & Laurent 2001,

DiCarlo et al. 2012) is to feed the activity of a small neuronal population into a much larger one—termed representational expansion (Cortes & Vapnik 1995). But such an expansion is not necessarily beneficial when the information in the small input representation is limited, as several studies have demonstrated (Series et al. 2004, Bejjanki et al. 2011, Babadi & Sompolinsky 2014).

A second issue is that visual processing requires relaying spiking activity through distributed networks, in which a cortical area may receive input from multiple competing sources. Modeling work has shown that relaying spiking activity reliably through such distributed networks can be surprisingly difficult (Salinas & Sejnowski 2000, Litvak et al. 2003, Vogels et al. 2005, Kumar et al. 2010, Zandvakili & Kohn 2015). This imposes an entirely different functional constraint on correlations—determining their potency in driving downstream networks, which may have their own rich, internal dynamics.

Ultimately, understanding the influence of correlations on brain function will require the study of spiking networks with an architecture that captures essential features of the biology and which implement the rich computations performed by those networks. The picture that would emerge from such an effort will surely build on the insights we have gained from studying the decoding of one-dimensional variables but will undoubtedly also raise entirely new sets of issues and constraints.

SUMMARY

Work in the past few decades has greatly advanced our understanding of how neuronal population information is influenced by correlations. Theoretical work has been instrumental in this progress. It has shown us that some forms of correlations limit information, whereas others do not. At least in the context of population information, theoretical progress has also revealed that simply characterizing response statistics can have limited value: Describing correlations does not translate into understanding information, as the largest correlations do not necessarily have the strongest effect on information. We view this progress as a cautionary tale because we are entering an era when our power to measure brain activity is exploding, while our conceptual frameworks remain underdeveloped. Our situation is perhaps analogous to pre-Newtonian physics, which attempted to understand the movements of the stars and planets through extremely careful and detailed measurements. Ultimately, however, orbits were understood in a straightforward way with Newtonian physics. We see a risk that we—like pre-Newtonian physicists, but abetted by much more powerful instrumentation—will drown in a sea of description, measuring and characterizing population activity patterns rather than understanding the computations and functions they underlie.

DISCLOSURE STATEMENT

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

ACKNOWLEDGMENTS

We thank Marlene Cohen and Robbe Goris for helpful comments. A.K. was supported by the US National Institutes of Health (EY016774 and EY024858), Irma T. Hirschl Trust, Simons Foundation (364994AK), and Research to Prevent Blindness. R.C.-C. was supported by a fellowship from the Swiss National Science Foundation (PAIBA3-145045). A.P. was supported by a grant from the Swiss National Science Foundation (#31003A_143707).

LITERATURE CITED

Abbott LF, Dayan P. 1999. The effect of correlated variability on the accuracy of a population code. *Neural Comput.* 11:91–101

Adibi M, McDonald JS, Clifford CWG, Arabzadeh E. 2013. Adaptation improves neural coding efficiency despite increasing correlations in variability. *J. Neurosci.* 33:2108–20

Adibi M, McDonald JS, Clifford CWG, Arabzadeh E. 2014. Population decoding in rat barrel cortex: optimizing the linear readout of correlated population responses. *PLOS Comput. Biol.* 10(1):e1003415

Arandia-Romero I, Tanabe S, Drugowitsch J, Kohn A, Moreno-Bote R. 2016. Multiplicative and additive modulation of neuronal tuning with population activity affects encoded information. *Neuron* 89(6):1305–16

Arieli A, Sterkin A, Grinvald A, Aertsen A. 1996. Dynamics of ongoing activity: explanation of the large variability in evoked cortical responses. *Science* 273:1868–71

Atick J, Redlich A. 1990. Towards a theory of early visual processing. *Neural Comput.* 2:308–20

Averbeck BB, Latham PE, Pouget A. 2006. Neural correlations, population coding and computation. *Nat. Rev. Neurosci.* 7:358–66

Babadi B, Sompolinsky H. 2014. Sparseness and expansion in sensory representations. *Neuron* 83:1213–26

Bair W1, Zohary E, Newsome WT. 2001. Correlated firing in macaque visual area MT: time scales and relationship to behavior. *J. Neurosci.* 21:1676–97

Baker PM, Bair W. 2012. Inter-neuronal correlation distinguishes mechanisms of direction selectivity in cortical circuit models. *J. Neurosci.* 32:8800–16

Barlow H. 2001. Redundancy reduction revisited. *Network* 12:241–53

Beck JM, Bejjanki VR, Pouget A. 2011. Insights from a simple expression for linear Fisher information in a recurrently connected population of spiking neurons. *Neural Comput.* 23:1484–502

Beck JM, Heller K, Pouget A. 2012a. Complex inference in neural circuits with probabilistic population codes and topic models. In *Advances in Neural Information Processing Systems*, Vol. 4, ed. P Bartlett, pp. 3068–76. Cambridge, MA: MIT Press

Beck JM, Ma WJ, Pitkow X, Latham PE, Pouget A. 2012b. Not noisy, just wrong: the role of suboptimal inference in behavioral variability. *Neuron* 74:30–39

Bejjanki VR, Beck JM, Lu ZL, Pouget A. 2011. Perceptual learning as improved probabilistic inference in early sensory areas. *Nat. Neurosci.* 14:642–48

Berens P, Ecker AS, Cotton RJ, Ma WJ, Bethge M, Tolias AS. 2012. A fast and simple population code for orientation in primate V1. *J. Neurosci.* 32:10618–26

Berkes P, Orbán G, Lengyel M, Fiser J. 2011. Spontaneous cortical activity reveals hallmarks of an optimal internal model of the environment. *Science* 331:83–87

Bosking WH, Zhang Y, Schofield B, Fitzpatrick D. 1997. Orientation selectivity and the arrangement of horizontal connections in tree shrew striate cortex. *J. Neurosci.* 17:2112–27

Bujan AF, Aertsen A, Kumar A. 2015. Role of input correlations in shaping the variability and noise correlations of evoked activity in the neocortex. *J. Neurosci.* 35:8611–25

Butts DA, Goldman MS. 2006. Tuning curves, neuronal variability, and sensory coding. *PLOS Biol.* 4(4):e92

Buzsaki G. 2006. *Rhythms of the Brain*. New York: Oxford Univ. Press

Calabrese A, Woolley SM. 2015. Coding principles of the canonical cortical microcircuit in the avian brain. *PNAS* 112:3517–22

Cohen MR, Kohn A. 2011. Measuring and interpreting neuronal correlations. *Nat. Neurosci.* 14:811–19

Cohen MR, Newsome WT. 2008. Context-dependent changes in functional circuitry in visual area MT. *Neuron* 60:162–73

Cohen MR, Maunsell JH. 2009. Attention improves performance primarily by reducing interneuronal correlations. *Nat. Neurosci.* 12:1594–600

Cortes C, Vapnik V. 1995. Support-vector networks. *Mach. Learn.* 20:273–97

Cossell L, Iacaruso MF, Muir DR, Houlton R, Sader EN, et al. 2015. Functional organization of excitatory synaptic strength in primary visual cortex. *Nature* 518:399–403

da Silveira RA, Berry MJ II. 2014. High-fidelity coding with correlated neurons. *PLOS Comput. Biol.* 10(11):e1003970

Dayan P, Abbott LF. 2001. *Theoretical Neuroscience*. Cambridge, MA: MIT Press
Deneve S, Latham PE, Pouget A. 1999. Reading population codes: a neural implementation of ideal observers. *Nat. Neurosci.* 2:740–45
Denman DJ, Contreras D. 2014. The structure of pairwise correlation in mouse primary visual cortex reveals functional organization in the absence of an orientation map. *Cereb. Cortex* 24:2707–20
DiCarlo JJ, Zoccolan D, Rust NC. 2012. How does the brain solve visual object recognition? *Neuron* 73:415–34
Doiron B, Litwin-Kumar A, Rosenbaum R, Ocker GK, Josić K. 2016. The mechanics of state-dependent neural correlations. *Nat. Neurosci.* 19(3):383–93
Ecker AS, Berens P, Cotton RJ, Subramaniyan M, Denfield GH, et al. 2014. State dependence of noise correlations in macaque primary visual cortex. *Neuron* 82:235–48
Ecker AS, Berens P, Keliris GA, Bethge M, Logothetis NK, Tolias AS. 2010. Decorrelated neuronal firing in cortical microcircuits. *Science* 327:584–87
Ecker AS, Berens P, Tolias AS, Bethge M. 2011. The effect of noise correlations in populations of diversely tuned neurons. *J. Neurosci.* 31:14272–83
Ecker AS, Denfield GH, Bethge M, Tolias AS. 2015. On the structure of population activity under fluctuations in attentional state. bioRxiv:018226
Fetsch CR, Pouget A, DeAngelis GC, Angelaki DE. 2011. Neural correlates of reliability-based cue weighting during multisensory integration. *Nat. Neurosci.* 15:146–54
Fiser J, Berkes P, Orbán G, Lengyel M. 2010. Statistically optimal perception and learning: from behavior to neural representations. *Trends Cogn. Sci.* 14:119–30
Foldiak P. 1993. The 'ideal homunculus': statistical inference from neural population responses. In *Computation and Neural Systems*, ed. F Eeckman, J Bower, pp. 55–60. Norwell, MA: Kluwer Acad.
Friedrich RW. 2013. Neuronal computations in the olfactory system of zebrafish. *Annu. Rev. Neurosci.* 36:383–402
Friedrich RW, Laurent G. 2001. Dynamic optimization of odor representations by slow temporal patterning of mitral cell activity. *Science* 291:889–94
Ganguli D, Simoncelli EP. 2014. Efficient sensory encoding and Bayesian inference with heterogeneous neural populations. *Neural Comput.* 26:2103–34
Gerhard F, Kispersky T, Gutierrez GJ, Marder E, Kramer M, Eden U. 2013. Successful reconstruction of a physiological circuit with known connectivity from spiking activity alone. *PLOS Comput. Biol.* 9(7):e1003138
Gerwinn S, Macke JH, Bethge M. 2010. Bayesian inference for generalized linear models for spiking neurons. *Front. Comput. Neurosci.* 4:12
Ginzburg II, Sompolinsky H. 1994. Theory of correlations in stochastic neural networks. *Phys. Rev. E.* 50:3171–91
Goris RL, Movshon JA, Simoncelli EP. 2014. Partitioning neuronal variability. *Nat. Neurosci.* 17:858–65
Grabska-Barwińska A, Beck J, Pouget A, Latham P. 2014. Demixing odors—fast inference in olfaction. In *Advances in Neural Information Processing Systems*, Vol. 24, ed. P Bartlett, pp. 1968–76. Cambridge, MA: MIT Press
Graf AB, Kohn A, Jazayeri M, Movshon JA. 2011. Decoding the activity of neuronal populations in macaque primary visual cortex. *Nat. Neurosci.* 14:239–45
Graupner M, Reyes AD. 2013. Synaptic input correlations leading to membrane potential decorrelation of spontaneous activity in cortex. *J. Neurosci.* 33:15075–85
Gu Y, Liu S, Fetsch CR, Yang Y, Fok S, et al. 2011. Perceptual learning reduces interneuronal correlations in macaque visual cortex. *Neuron* 71:750–61
Gutnisky DA, Dragoi V. 2008. Adaptive coding of visual information in neural populations. *Nature* 452:220–24
Haefner RM, Berkes P, Fiser J. 2014. Perceptual decision-making as probabilistic inference by neural sampling. arXiv:1409.0257 [q-bio.NC]
Haefner RM, Gerwinn S, Macke JH, Bethge M. 2013. Inferring decoding strategies from choice probabilities in the presence of correlated variability. *Nat. Neurosci.* 16:235–42
Hansen BJ, Chelaru MI, Dragoi V. 2012. Correlated variability in laminar cortical circuits. *Neuron* 76:590–602
Harris KD, Thiele A. 2011. Cortical state and attention. *Nat. Rev. Neurosci.* 12:509–23

Hennequin G, Aitchison L, Lengyel M. 2014. Fast sampling-based inference in balanced neuronal networks. In *Advances in Neural Information Processing Systems*, Vol. 27, ed. P Bartlett, pp. 2240–48. Cambridge, MA: MIT Press

Herrero JL, Gieselmann MA, Sanayei M, Thiele A. 2013. Attention-induced variance and noise correlation reduction in macaque V1 is mediated by NMDA receptors. *Neuron* 78:729–39

Hirabayashi T, Takeuchi D, Tamura T Miyashita Y. 2013. Microcircuits for hierarchical elaboration of object coding across primate temporal areas. *Science* 341:191–95

Huang X, Lisberger SG. 2009. Noise correlations in cortical area MT and their potential impact on trial-by-trial variation in the direction and speed of smooth-pursuit eye movements. *J. Neurophysiol.* 101:3012–30

Jazayeri M, Movshon JA. 2006. Optimal representation of sensory information by neural populations. *Nat. Neurosci.* 9:690–96

Jeanne JM, Sharpee TO, Gentner TQ. 2013. Associative learning enhances population coding by inverting interneuronal correlation patterns. *Neuron* 78:352–63

Jorgenson LA, Newsome WT, Anderson DJ, Bargmann CI, Brown EN, et al. 2015. The BRAIN Initiative: developing technology to catalyse neuroscience discovery. *Philos. Trans. R. Soc. B* 370:20140164

Kanitscheider I, Coen-Cagli R, Kohn A, Pouget A. 2015a. Measuring Fisher information accurately in correlated neural populations. *PLOS Comput. Bio.* 11(6):e1004218

Kanitscheider I, Coen-Cagli R, Pouget A. 2015b. The origin of information-limiting correlations. *PNAS.* 112:E6973–82

Kohn A, Smith MA. 2005. Stimulus dependence of neuronal correlation in primary visual cortex of the macaque. *J. Neurosci.* 25:3661–73

Kohn A, Zandvakili A, Smith MA. 2009. Correlations and brain states: from electrophysiology to functional imaging. *Curr. Opin. Neurobiol.* 19:434–38

Komiyama T, Sato TR, O'Connor DH, Zhang YX, Huber D, et al. 2010. Learning-related fine-scale specificity imaged in motor cortex circuits of behaving mice. *Nature* 464:1182–86

Kumar A, Rotter S, Aertsen A. 2010. Spiking activity propagation in neuronal networks: reconciling different perspectives on neural coding. *Nat. Rev. Neurosci.* 11:615–27

Lin IC, Okun M, Carandini M, Harris KD. 2015. The nature of shared cortical variability. *Neuron* 87:644–56

Litvak V, Sompolinsky H, Segev I, Abeles M. 2003. On the transmission of rate code in long feedforward networks with excitatory-inhibitory balance. *J. Neurosci.* 23:3006–15

Litwin-Kumar A, Doiron B. 2012. Slow dynamics and high variability in balanced cortical networks with clustered connections. *Nat. Neurosci.* 15:1498–1505

Ma WJ, Beck JM, Latham PE, Pouget A. 2006. Bayesian inference with probabilistic population codes. *Nat. Neurosci.* 9:1432–38

Martin KA, Schroder S. 2013. Functional heterogeneity in neighboring neurons of cat primary visual cortex in response to both artificial and natural stimuli. *J. Neurosci.* 33:7325–44

Masud MS, Borisyuk R. 2011. Statistical technique for analysing functional connectivity of multiple spike trains. *J. Neurosci. Methods* 196:201–19

McDonald JS, Clifford CW, Solomon SS, Chen SC, Solomon SG. 2014. Integration and segregation of multiple motion signals by neurons in area MT of primate. *J. Neurophysiol.* 111:369–78

Mitchell JF, Sundberg KA, Reynolds JH. 2009. Spatial attention decorrelates intrinsic activity fluctuations in macaque area V4. *Neuron* 63:879–88

Moore GP, Segundo JP, Perkel DH, Levitan H. 1970. Statistical signs of synaptic interactions in neurons. *Biophys. J.* 10:876–900

Moreno-Bote R, Beck J, Kanitscheider I, Pitkow X, Latham P, Pouget A. 2014. Information-limiting correlations. *Nat. Neurosci.* 17:1410–17

Nienborg H, Cohen MR, Cumming BG. 2012. Decision-related activity in sensory neurons: correlations among neurons and with behavior. *Annu. Rev. Neurosci.* 35:463–83

Ohiorhenuan IE, Mechler F, Purpura KP, Schmid AM, Hu Q, Victor JD. 2010. Sparse coding and high-order correlations in fine-scale cortical networks. *Nature* 466:617–21

Okatan M, Wilson MA, Brown EN. 2005. Analyzing functional connectivity using a network likelihood model of ensemble neural spiking activity. *Neural Comput.* 17:1927–61

Okun M, Steinmetz NA, Cossell L, Iacaruso MF, Ko H, et al. 2015. Diverse coupling of neurons to populations in sensory cortex. *Nature* 521:511–15

Ostojic S. 2014. Two types of asynchronous activity in networks of excitatory and inhibitory spiking neurons. *Nat. Neurosci.* 17:594–600

Ostojic S, Brunel N, Hakim V. 2009. How connectivity, background activity, and synaptic properties shape the cross-correlation between spike trains. *J. Neurosci.* 29:10234–53

Pachitariu M, Lyamzin DR, Sahani M, Lesica NA. 2015. State-dependent population coding in primary auditory cortex. *J. Neurosci.* 35:2058–73

Paradiso MA. 1988. A theory for the use of visual orientation information which exploits the columnar structure of striate cortex. *Biol. Cybern.* 58:35–49

Pillow JW, Shlens J, Paninski L, Sher A, Litke AM, et al. 2008. Spatio-temporal correlations and visual signalling in a complete neuronal population. *Nature* 454:995–99

Pitkow X, Liu S, Angelaki DE, DeAngelis GC, Pouget A. 2015. How can single sensory neurons predict behavior? *Neuron* 87:411–23

Pouget A, Beck JM, Ma WJ, Latham PE. 2013. Probabilistic brains: knowns and unknowns. *Nat. Neurosci.* 16:1170–78

Pouget A, Dayan P, Zemel R. 2000. Information processing with population codes. *Nat. Rev. Neurosci.* 1:125–32

Pouget A, Thorpe S. 1991. Connectionist model of orientation identification. *Connect. Sci.* 3:127–42

Poulet JF, Petersen CC. 2008. Internal brain state regulates membrane potential synchrony in barrel cortex of behaving mice. *Nature* 454:881–85

Rabinowitz NC, Goris RL, Cohen M, Simoncelli EP. 2015. Attention stabilizes the shared gain of V4 populations. *eLife* 2(4):e08998

Ramalingam N, McManus JNJ, Li W, Gilbert CD. 2013. Top-down modulation of lateral interactions in visual cortex. *J. Neurosci.* 33:1773–89

Rasch MJ, Schuch K, Logothetis NK, Maass W. 2011. Statistical comparison of spike responses to natural stimuli in monkey area V1 with simulated responses of a detailed laminar network model for a patch of V1. *J. Neurophysiol.* 105:757–78

Reid RC, Alonso JM. 1995. Specificity of monosynaptic connections from thalamus to visual cortex. *Nature* 378:281–84

Renart A, de la Rocha J, Bartho P, Hollender L, Parga N, et al. 2010. The asynchronous state in cortical circuits. *Science* 327:587–90

Renart A, van Rossum MC. 2012. Transmission of population-coded information. *Neural Comput.* 24:391–407

Rescorla RA, Wagner AR. 1972. A theory of Pavlovian conditioning: the effectiveness of reinforcement and non-reinforcement. In *Classical Conditioning II: Current Research and Theory*, ed. AH Black, WF Prokasy, pp. 64–69. New York: Appleton-Century-Crofts

Roelfsema PR, Lamme VA, Spekreijse H. 2004. Synchrony and covariation of firing rates in the primary visual cortex during contour grouping. *Nat. Neurosci.* 7:982–91

Ruff DA, Cohen MR. 2014. Attention can either increase or decrease spike count correlations in visual cortex. *Nat. Neurosci.* 17:1591–97

Salinas E, Abbott LF. 1994. Vector reconstruction from firing rates. *J. Comput. Neurosci.* 1:89–107

Salinas E, Sejnowski TJ. 2000. Impact of correlated synaptic input on output firing rate and variability in simple neuronal models. *J. Neurosci.* 20:6193–6209

Sanger T. 1996. Probability density estimation for the interpretation of neural population codes. *J. Neurophys.* 76:2790–2793

Sato TK, Nauhaus I, Carandini M. 2012. Traveling waves in visual cortex. *Neuron* 75:218–29

Schneidman E, Berry MJ II, Segev R, Bialek W. 2006. Weak pairwise correlations imply strongly correlated network states in a neural population. *Nature* 440:1007–12

Schölvinck ML, Saleem AB, Benucci A, Harris KD, Carandini M. 2015. Cortical state determines global variability and correlations in visual cortex. *J. Neurosci.* 35:170–78

Seriès P, Latham PE, Pouget A. 2004. Tuning curve sharpening for orientation selectivity: coding efficiency and the impact of correlations. *Nat. Neurosci.* 7:1129–35

Seung HS, Sompolinsky H. 1993. Simple models for reading neuronal population codes. *PNAS* 90:10749–53

Shadlen MN, Newsome WT. 1998. The variable discharge of cortical neurons: implications for connectivity, computation, and information coding. *J. Neurosci.* 18:3870–96

Shamir M, Sompolinsky H. 2004. Nonlinear population codes. *Neural Comput.* 16:1105–36

Shamir M, Sompolinsky H. 2006. Implications of neuronal diversity on population coding. *Neural Comput.* 18:1951–86

Simoncelli EP, Olshausen BA. 2001. Natural image statistics and neural representation. *Annu. Rev. Neurosci.* 24:1193–1216

Smith MA, Jia X, Zandvakili A, Kohn A. 2013. Laminar dependence of neuronal correlations in visual cortex. *J. Neurophysiol.* 109:940–47

Smith MA, Kohn A. 2008. Spatial and temporal scales of neuronal correlation in primary visual cortex. *J. Neurosci.* 28:12591–603

Smith MA, Sommer MA. 2013. Spatial and temporal scales of neuronal correlation in visual area V4. *J. Neurosci.* 33:5422–32

Solomon SS, Chen SC, Morley JW, Solomon SG. 2014. Local and global correlations between neurons in the middle temporal area of primate visual cortex. *Cereb. Cortex* 25:3182–96

Sompolinsky H, Yoon H, Kang K, Shamir M. 2001. Population coding in neuronal systems with correlated noise. *Phys. Rev. E.* 64:051904

Song S, Sjöström PJ, Reigl M, Nelson S, Chklovskii DB. 2005. Highly nonrandom features of synaptic connectivity in local cortical circuits. *PLOS Biol.* 3(3):e68

Stevenson IH, Rebesco JM, Miller LE, Körding KP. 2008. Inferring functional connections between neurons. *Curr. Opin. Neurobiol.* 18:582–88

Tan AY, Chen Y, Scholl B, Seidemann E, Priebe NJ. 2014. Sensory stimulation shifts visual cortex from synchronous to asynchronous states. *Nature* 509:226–29

Tolhurst DJ, Movshon JA, Dean AF. 1983. The statistical reliability of signals in single neurons in cat and monkey visual cortex. *Vis. Res.* 23:775–85

van Vreeswijk C, Sompolinsky H. 1996. Chaos in neuronal networks with balanced excitatory and inhibitory activity. *Science* 274:1724–26

Vogels TP, Abbott LF. 2005. Signal propagation and logic gating in networks of integrate-and-fire neurons. *J. Neurosci.* 25:10786–95

Vogels TP, Rajan K, Abbott LF. 2005. Neural network dynamics. *Annu. Rev. Neurosci.* 28:357–76

Widrow B, Hoff ME Jr. 1960. Adaptive switching circuits. *IRE WESCON Conv. Rec.* 4:96–104

Wilke SD, Eurich CW. 2002. Representational accuracy of stochastic neural populations. *Neural Comput.* 14:155–89

Wimmer K, Compte A, Roxin A, Peixoto D, Renart A, de la Rocha J. 2015. Sensory integration dynamics in a hierarchical network explains choice probabilities in cortical area MT. *Nat. Commun.* 6:6177

Wu S, Nakahara H, Amari S. 2001. Population coding with correlation and an unfaithful model. *Neural Comput.* 13:775–97

Yoshimura Y, Dantzker JLM, Callaway EM. 2005. Excitatory cortical neurons form fine-scale functional networks. *Nature* 433:868–73

Yu BM, Kohn A, Smith MA. 2011. *Estimating shared firing rate fluctuations in neural populations*. Program No. 483.18/NN1. Presented at Soc. Neurosci., Nov. 14, Washington DC.

Yu J, Ferster D. 2013. Functional coupling from simple to complex cells in the visually driven cortical circuit. *J. Neurosci.* 33:18855–66

Zandvakili A, Kohn A. 2015. Coordinated neuronal activity enhances corticocortical communication. *Neuron* 87:827–39

Zohary E, Shadlen MN, Newsome WT. 1994. Correlated neuronal discharge rate and its implications for psychophysical performance. *Nature* 370:140–43