

An uncorrelated state for the cortex?

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Abstract

The spike trains of nearby neurons in the sensory cortex are typically thought to be correlated due to mutual connections and common input. Multiple studies have measured these correlations and found them to be substantial (in the range of 10-40%). Two recent papers, however, reported that average correlations can be an order of magnitude smaller. Such low correlations could indicate an 'uncorrelated state' for the cortex, where cortical neurons act independently even in the face of strong common input.

Introduction and context

The correlation between the activity of neurons in the sensory cortex has long been the object of interest, as its measurement allows inferences about underlying anatomical connectivity [1]. A peak in the cross-correlogram between the firing rates of two neurons can indicate a monosynaptic connection or common input [2]. This technique, for instance, is in wide use to study functional connectivity within the primary visual cortex [3] (e.g., to investigate horizontal connections [4] or connections between simple and complex cells [5]).

Knowing the correlation between neurons can also serve to constrain the possible schemes employed by the cortex to code and decode sensory stimuli [6-8]. Intuitively, it may not seem advantageous to maintain millions of neurons if their activity is highly correlated. The impact of correlations on decoding accuracy, however, depends on the decoding scheme. For a decoder that performs simple averages, correlations are deleterious and would limit behavioural performance [6,9-11].

The appropriate methods for measuring correlation depend on what is being studied. Under truly stationary conditions (i.e., in the absence of a stimulus and of global modulations of responsiveness), it is sufficient to

compute a simple correlation coefficient. A stimulus introduces a trivial correlation among neurons, which depends on their stimulus selectivity. This 'stimulus correlation' is usually removed by subtracting the 'shuffle predictor' [1], which is the cross-correlogram of trial-averaged responses [10]. What remains after subtraction is the 'noise correlation' and is typically the quantity of interest. Correlations due to changes in the global state activity, in turn, are harder to remove because such changes are typically not repeatable and are hard to identify. Changes in global activity are therefore usually ignored, an approach fraught with peril because their impact on the measured correlation can be substantial [12].

Using these methods, most studies to date have reported significant correlations among cortical neurons. The exact value of the correlation depends heavily on a variety of factors, including the time scale over which it is computed [10,13], the firing rates of the neurons [14], the distance and difference in tuning between the neurons [10,13,15], the strength of the sensory stimulus [13,16], the past history of stimulation [17], and the behavioural condition in terms of arousal and attention [18]. Nonetheless, these and other studies have found that in most conditions the correlations are positive and substantial, with average values in the range of 10-40%.

Major recent advances

Surprisingly, two recent studies reported that average correlations in the sensory cortex can be 10 times lower [19,20]. Ecker and colleagues [19] measured average correlations in the primary visual cortex of awake macaques and found the correlation to be in the order of 1%. This is particularly surprising as the authors binned the data in long windows (500 ms), and such long windows, if anything, bias correlation toward higher values. Working in somatosensory and auditory cortices of anaesthetized rodents, Renart *et al.* [20] reported that average correlations depend on the state of the cortex. Extremely low correlations – again, in the range of 1% – were seen during ‘activated states’, which are devoid of up-down fluctuations [21,22].

A remarkable aspect of these two new studies [19,20] is that correlations between pairs of neurons were about as likely to be positive as to be negative (thereby yielding an average of close to zero). This is in sharp contrast to most other studies [10,13-15,17], which found predominantly positive correlations (and thus positive averages).

Given that cortical neurons are likely to receive substantial common input, extremely low average correlations need explanation. This explanation may come from the theory of balanced networks [23,24], which was developed to explain how an interconnected network can inhabit regimes intermediate between complete silence and full-on epilepsy. A balanced network postulates connections (typically random) between and within two pools of excitatory and inhibitory cells. In such a network, recurrent inhibition closely tracks excitation with a small lag. Such tracking generates negative correlations in synaptic currents and these negative correlations cancel existing positive correlations, including those due to common input [20].

Thanks to this intuition, Renart *et al.* [20] show that average correlations between neurons can be very small, not only in the sparsely connected networks studied previously, but also in densely connected networks with strong coupling and substantial common input. The authors show that, in such a network, the population-averaged correlation decreases as the inverse of the number of neurons.

A network where correlations are extremely weak is said to be in an ‘asynchronous state’ [20,23], but in neuroscience, synchrony usually refers only to time scales of milliseconds (e.g., [25]). A more appropriate term might be an ‘uncorrelated state’.

Future directions

Have these two studies discovered a cortical state that had eluded previous investigations? What are the key factors that explain these large differences in correlation relative to the previous studies?

One possible factor lies in global modulations in activity. These global modulations can have a large impact on measured correlations [12] and are common not only under some forms of anaesthesia but also in awake animals [26-28]. These global modulations may perhaps have been lower in the animals in the study by Ecker *et al.* [19]. Renart *et al.* [20] measured the global modulations and thus were able to concentrate on the activated state. Conversely, when the authors included data showing up-down fluctuations, the average correlation between neurons rose substantially.

Other factors that may contribute to the low correlations seen in the study of the visual cortex are the size and strength of the stimulus. Ecker *et al.* [19] used a high-contrast visual stimulus, and it is well established that such stimuli decrease neuronal correlation [13,16]. It would be interesting to know to what extent the stimulus influenced the low values of correlation that were measured.

Very recently, a possible factor for the discrepancy in measured correlations was identified in the laminar structure of the cortex. Smith and Kohn [29] measured spike count correlation between pairs of neurons at various depths in the primary visual cortex and found a striking dependence on cortical layer. Correlation between neurons in the superficial or deep layers could be as high as in the previous studies (in excess of 10%), but correlation between neurons in the intermediate layers was extremely low (as low as 2%). Knowledge of the layers in which the various studies have made recordings may explain the discrepancy between their measures of correlation.

A future challenge will be to identify clearly the temporal [10,15] and spatial scales [15] of cortical correlation and to investigate their dependence on stimulus attributes such as contrast [13,16] and on cognitive factors such as attention [18,27,30]. More generally, the results of Ecker *et al.* [19] and Renart *et al.* [20] put into question the utility of using noise correlation to investigate cortical connectivity. It may be more useful to develop generative models of neural responses which will include the effects of incoming stimuli, of common inputs, and of lateral connections [31]. By predicting the spike trains of individual

neurons accurately, these models would also predict their noise correlation (or lack thereof) and thereby provide insight into the underlying mechanisms.

Competing interests

The authors declare that they have no competing interests.

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