The impact of high order interactions on the rate of synchronous discharge and information transmission in somatosensory cortex

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Understanding the operations of neural networks in the brain requires an understanding of whether interactions among neurons can be described by a pairwise interaction model, or whether a higher order interaction model is needed. In this article we consider the rate of synchronous discharge of a local population of neurons, a macroscopic index of the activation of the neural network that can be measured experimentally. We analyze a model, based on physics' maximum entropy principle, that evaluates whether the probability of synchronous discharge can be described by interactions up to any given order. When compared with real neural population activity obtained from the rat somatosensory cortex, the model shows that interactions of at least order three or four are necessary to explain the data. We use Shannon information to compute the impact of high order correlations on the amount of somatosensory information transmitted by the rate of synchronous discharge, and we found that correlations of higher order progressively decreased the information available through the neural population. These results are compatible with the hypothesis that high order interactions play a role in shaping the dynamics of neural networks, and that they should be taken into account when computing the representational capacity of neural populations.

Keywords: Spike Synchronization; Mutual Information; Information Geometry; Maximum Entropy

1. Introduction

Simultaneous recordings of the activity of individual neurons placed within local networks in the central nervous system show that a large fraction of pairs of neu-

rons are correlated. The probability of observing near-simultaneous spikes from two different neurons is often significantly higher than the product of the probability of observing the individual spikes from each neuron (Li *et al.*, 1959; Perkel *et al.*, 1969; Mastronarde, 1983).

The ubiquitous presence of correlations among the activity of different neurons has raised the question of what is the impact of correlation upon neural population coding of sensory stimuli (see (Averbeck *et al.*, 2006 ; Salinas *et al.*, 2001) for recent reviews). Although the potential role of correlations in neural population codes is still unclear and robustly debated (Shadlen & Movshon, 1999; von der Malsburg, 1999), theoretical studies have suggested that correlations can profoundly affect the information transmitted by neural populations. On the one hand, correlations may play a crucial and beneficial role in the neural code, by increasing the information content of neural populations (Abbot & Dayan, 1999; Oram *et al.*, 1998; Pola *et al.*, 2003), by serving as a scheme for implementing associations and binding of features (von der Malsburg, 1999) or by implementing strategies for error correction (Schneidman *et al.*, 2006). On the other hand, correlations may reflect correlated noise arising from the structure of cortical circuits, and may act as a detrimental, limiting factor to the representational capacity of neural populations (Zohary *et al.*, 1994; Mazurek & Shadlen, 2002). Whether correlations give a positive or negative contribution depends on the precise details of the correlational structure of neural activity (Abbot & Dayan, 1999; Oram *et al.*, 1998; Pola *et al.*, 2003). Determining the precise structure of correlated activity is thus crucial for the progress of systems neuroscience.

A particularly important question about the structure of correlated activity of large neural populations is whether it can be described by considering only pairwise interactions, or if genuine high order interactions between neurons are present. The understanding of the role of high order interactions is important for several reasons. First, most studies of population codes are based on the recording of neural pairs and of pairwise correlations (Panzeri *et al.*, 1999; Nirenberg *et al.*, 2001; Panzeri *et al.* 2001; Petersen *et al.*, 2001; Montani *et al.*, 2007). Pairwise studies can only inform about the behavior of large populations if higher order interactions are absent. Second, the presence of high order interactions has implications for the understanding of the functional organization of neural networks in the brain (Martignon *et al.*, 2000), because high order interactions are compatible with information transmission by activation of tightly connected cell assemblies (Harris, 2005). Third, understanding which is the minimal order of interaction sufficient to describe correlations among neurons is crucial to develop simple but effective models of decoding of neural population activity (Nirenberg & Victor, 2007). This question is only now beginning to be addressed both at the theoretic level (Bohte *et al.*, 2000; Nakahara & Amari, 2002; Amari *et al.*, 2003) and the experimental level (Shlens *et al.*, 2006; Schneidman *et al.*, 2006; Tang *et al.*, 2008).

In this study we evaluate the presence of high order correlations in the somatosensory cortical network, by investigating whether the observed probability of synchronous firing to a given sensory stimulus can only be explained by considering high order interactions, and whether such high order interactions play a role in transmission of information about the stimuli.

2. Information Geometry and the probability of synchronous discharge in an homogeneous neural population

We consider a population of N neurons whose activity is simultaneously observed during a specified short time window of size Δt following the presentation of a sensory stimulus s taken from a set of S different stimuli. We represent neuronal population activity by a binary vector $\mathbf{x} = (x_1, ..., x_N)$ in the space X of all binary vectors of length N, where $x_i = 0$ if neuron i is silent in some time window and $x_i = 1$ if it is firing one or more spikes. The probability distribution $P(\mathbf{x}|s)$ of observing population response conditional to the presentation of stimulus s can be expressed using different coordinate systems. The most obvious way of characterising such a distribution is by specifying the $2^N - 1$ individual probability values; these are called the p-coordinates. Alternatively, the probability can be determined by the $2^N - 1$ marginal probability values; these are called the η-coordinates (Amari 2001). Provided $P(\mathbf{x}|s) \neq 0$ for any $\mathbf{x}$, any such distribution can be expanded in the so-called log-linear model, or θ-coordinates system (Amari, 2001; Nakahara & Amari, 2002; Martignon *et al.*, 2000):

$$P(\mathbf{x}|s) = \exp \left\{ \sum x_i \hat{\theta}_i + \sum_{i<j} x_i x_j \hat{\theta}_{ij} + \right. \tag{2.1}$$

$$\left. \sum_{i<j<k} x_i x_j x_k \hat{\theta}_{ijk} + ... + \sum_{i<...<N} x_i...x_N \hat{\theta}_{i...N} - \psi \right\}$$

where the $2^N - 1$ different $\hat{\theta}$ coefficients uniquely determine the distribution and are, at least in principle, stimulus dependent (although in the following their stimulus dependence will be dropped for notational simplicity). The use of this coordinate system to study probabilities and interactions was pioneered in the early eighties by Amari and coworkers (Amari, 1980; Amari, 1982), and then was later refined by the same authors (Amari & Nagaoka, 2000; Amari, 2001), in part thanks to the influential work of Curado and Tsallis (Curado & Tsallis, 1994) in developing a generalized theory of statistical mechanics. In this article, we will use the above θ-coordinate system because (as demonstrated in (Amari 2001) and discussed in the next section) it is the most natural coordinate system to study interactions between variables.

In order to simplify the analysis, and following previous theoretical work (Bohte *et al.*, 2000; Amari *et al.*, 2003), we will make a strong assumption about the neural population. We assume that the neural population is a fully homogeneous pool; that is all the parameters characterizing single neuron properties and interactions between any group of neurons do not depend on the precise identity of the considered neurons, but only on the number of neurons considered. With this assumption the probability distribution is now characterised by only N parameters. Due to the symmetry of the population all the θ-coordinates of a given order, k, are equal and can be represented by θ_k. For example, all interaction coefficients at order 3, $\hat{\theta}_{ijk}$, are equal to a single parameter that we indicate by θ_3. Under the homogeneous

pool assumption, Eq. (2.1) becomes:

$$P(\mathbf{x}|s) = \exp\left\{\sum x_i \theta_1 + \sum_{i<j} x_i x_j \theta_2 + \right. \tag{2.2}$$

$$\left. \sum_{i<j<k} x_i x_j x_k \theta_3 + ... + \sum_{i<...<N} x_i ... x_n \theta_N - \psi \right\}$$

Since the neurons are identical, the probabilities of all responses with m neurons firing are equal to each other. Thus, from the conditional distribution $P(\mathbf{x}|s)$ of the population response conditional to stimulus s, it is convenient to extract a simpler but still relevant probability distribution: the distribution $P(m|s)$ of the number m from the space $M = \{0, 1, ..., N\}$ of neurons simultaneously firing in response to stimulus s during the considered post-stimulus time interval. In the rest of the paper, we will denote m as the rate of coincident firing (because it is proportional to the fraction of active neurons at any given time). Due to the homogeneity assumption, $P(\mathbf{x}|s)$ and $P(m|s)$ are simply related by combinatorial factors and $P(m|s)$ is given by the following:

$$P(m|s) = \sum_{\mathbf{x} \in X_m} P(\mathbf{x}|s) \tag{2.3}$$

$$= \binom{N}{m} P(x_1 = \cdots = x_m = 1; x_{m+1} = \cdots = x_N = 0|s)$$

where X_m is the set of all vectors $\mathbf{x}$ containing exactly m cells firing. Hence equation (2.1) becomes:

$$P(m|s) = \binom{N}{m} e^{\left\{\sum_{i=1}^{m} \binom{m}{i} \cdot \theta_i - \psi(\theta)\right\}} \tag{2.4}$$

θ_i represents the effect on the log-probability of interactions of order i in the neuronal pool. The marginals η_m, which are the probabilities of any m particular neurons firing at the same time are (Bohte *et al.*, 2000)

$$\eta_m = \sum_{i=m}^{N} \binom{N-m}{i-m} \frac{P(i)}{\binom{N}{i}} \tag{2.5}$$

The probability of the number of neurons coincidentally firing is of physiological interest, because the number of near coincident inputs to a cell postsynaptic to the considered neural population is likely to be a key factor in determining the probability of firing of the postsynaptic cell (Softky, 1995; König *et al.*, 1996). Thus, the probability of coincident firing is likely to play a role in the actual information transmission as well as in the information representation.

The assumption of a homogeneous neural pool is of course an oversimplification of the properties of real neural networks and strongly limits the domain of applicability of this formalism. It is however crucial to allow us to robustly study the response probabilities of relatively large neural populations (a few tens of neurons) at fixed stimuli. The analysis of tens of neurons would be more problematic

when considering the full non-homogeneous model (Eq. 2.1), both because of computational problems (Martignon *et al.*, 2000) and data sampling issues (Panzeri *et al.*, 2007) related to the larger number of parameters to be estimated in the non-homogeneous model. Fortunately, the neural populations to which we will apply our analysis are relatively well described by the homogeneous-pool assumptions, as we will discuss below.

3. Investigating the order of interaction through the maximum entropy principle

A rigorous way to investigate the effects of different orders of interaction is provided by the technique of *maximum entropy*, which was originally introduced in statistical physics (Jaynes, 1957), and is now beginning to be used in neuroscience (Martignon *et al.*, 2000; Schneidman *et al.*, 2006; Shlens *et al.*, 2006; Tang *et al.*, 2006; Nirenberg & Victor, 2007; Montemurro *et al.*, 2007).

The idea of the maximum entropy (ME) principle is to first fix some constraints that are of interest. We then seek the simplest, or most random, distribution subject to those constraints. This removes all types of correlation or structure in the data that does not result from the constrained features. Since entropy is a measure of randomness, looking for the most random distribution corresponds to looking for the distribution with maximal entropy.

Here we use the ME principle to address the problem of what is the order of interactions among neurons which is sufficient to describe the probabilities of neural response. We will consider the distribution $P^{(k)}(\mathbf{x}|s)$ with maximum entropy within the class of all distributions with the same marginals up to order k as the real measured distribution $P(\mathbf{x}|s)$. The ME condition ensures that, though interactions of up to order k are preserved, there are no higher order interactions present. We can then compare these ME models for different orders to the real measured distribution. In practice, the comparison will be done on the lower-dimensional probability distribution of coincident firing $P^{(k)}(m|s)$ and $P(m|s)$, which under the homogeneity assumption are univocally related to $P^{(k)}(\mathbf{x}|s)$ and $P(\mathbf{x}|s)$ through simple combinatorial factors, as given in Eq. (2.3).

The log-linear form using θ-coordinates (Eqs. 2.2, 2.4) provides a convenient framework with which to obtain the maximum entropy distributions. The general form of the maximum entropy solution subject to constraints (Cover & Thomas, 1991) has the same form as the log-linear model, and it has been shown (Amari *et al.*, 2001) that, subject to constraints on the marginals of the distribution of up to order k, the maximum entropy solution is given by equation (2.2) with the model truncated to include only θ's of up to order k. Thus, it is possible to leverage the co-ordinate systems described above and the transformations between them to efficiently compute the maximum entropy solutions.

For a given order k, we compute the maximum entropy solutions as follows (more details given in (Ince *et al.*, 2009)). We start by matching interactions up to order k to those of the measured distribution by setting the low order η-coordinates of the maximum entropy solution to equal those of the measured distribution. Then, following (Amari, 2001; Amari *et al*, 2003), the maximum entropy solution among the distribution with the appropriate low order marginals is found by setting the high order components of the θ-coordinates to zero.

As shown in (Amari, 2001; Amari *et al* 2003), by enforcing both of these constraints simultaneously we obtain a set of simultaneous equations. The coordinate transformation from p to η-coordinates is given by equation (2.5) and denoted $\check{\eta}(\cdot)$. The coordinate transformation from θ to p-coordinates is given by equation (2.4) and denoted $\check{p}(\cdot)$. The maximum entropy requirement is enforced by setting $\bar{\theta}_{k+} = \{\bar{\theta}_i\}_{i>k} = 0$ where $\bar{\theta}_i$ are the θ-coordinates of the maximum entropy model. The maximum entropy distribution is then completely determined by the $\bar{\theta}_{k-} = \{\bar{\theta}_i\}_{i\leq k}$. These can be obtained through numerical solution of the following equation

$$\eta_{k^-} - \check{\eta}_{k^-}\left(\check{\mathbf{p}}\left(\bar{\theta}_{k-}, \bar{\theta}_{k+} = 0\right)\right) = \mathbf{0} \tag{3.1}$$

where $\eta_{k^-} = \{\eta_i\}_{i\leq k}$ of the measured distribution. This is a system of k equations in k unknowns. The Jacobian of this function can also be obtained analytically allowing efficient solution using a range of numerical optimization methods. Here we solve it by employing a least-squares approach using a Levenberg-Marquandt algorithm (Jones *et al.* 2001). Using this we are able to solve for orders up to ~ 10 for populations of ~ 30 cells in a few minutes on a laptop computer. Solutions of all orders are possible, but computation time grows exponentially with the order considered.

It is important to note that we maximize the entropy of the distribution of the population response $\mathbf{x}$, over the probabilities defined on the space X and given the constraints on marginals of up to order k. We do not maximize the entropy of the distribution of the rate of coincident firing m. This is correct because we want to impose *no interactions among neurons* apart form those fixed by the marginals of up to level k, and the interactions among neurons are defined in the population response space X. The entropy of the stimulus-conditional population response $H[\mathbf{X}|s]$ is not equal to the entropy of the rate of coincident firing $H[\mathbf{M}|s]$. In addition, the relationship between the two is not monotonic, so maximising $H[\mathbf{X}|s]$, does not result in $H[\mathbf{M}|s]$ being maximal. However, a relationship between the two entropies can be derived, using Eq (2.3):

$$\begin{aligned} H[\mathbf{X}|s] &= -\sum_m \sum_{\mathbf{x}\in X_m} \frac{P(m|s)}{\binom{N}{m}} \log_2 \frac{P(m|s)}{\binom{N}{m}} \\ &= H[\mathbf{M}|s] + \sum_m P(m|s) \log_2 \binom{N}{m} \end{aligned} \tag{3.2}$$

Since the relationship is not monotonic, it is possible that a distribution which has maximum entropy on the population responses $\mathbf{x}$ is not a maximum entropy distribution of the rate of coincident firing m. For example, as noted in (Amari *et al.*, 2003), the model where all neurons are independent from each other is a model of maximum entropy given the single-neuron marginal probability but it leads to a fully concentrated distribution of the number of coincidentally active neurons in the large N limit.

4. Predictions from theoretical analyses of the distribution of synchronous discharge in homogenous populations

Recent seminal theoretical articles using the ME principle (Bohte *et al.*, 2000; Amari *et al.*, 2003) have begun to elucidate the effect of high order interactions on the probability of the number of synchronously firing neurons $P(m|s)$. Particular important predictions come from the work of (Amari *et al.*, 2003), in which the authors consider the behavior of $P(m|s)$ in the thermodynamic (large N) limit. They found that, in the absence of correlations, $P(m|s)$ is concentrated around its mean due to the central limit theorem. They analyzed what conditions are required to obtain a widespread distribution, in which (even in the thermodynamic limit) different numbers of neurons simultaneously firing are possible. They found that even when pairwise or third order interactions are considered, the concentration is not resolved. Weak interactions at all orders are needed to obtain widespread distributions.

These predictions assign a strong role to high order interactions for all neural systems exhibiting widespread distribution of synchronous firing. Since these predictions are obtained in the thermodynamic limit, it is difficult to test these predictions on real data because the number of simultaneously recorded neurons in a typical experiment is small (up to a few tens of neurons at best). However, it is interesting to consider whether real data tend to produce concentrated or widespread distributions, and whether observed widespread distributions require high order interactions in order to be explained. We address this question directly in the next section.

5. The role of high order correlations in shaping synchronous discharge in somatosensory cortex

We apply the techniques described above related to a pooled population of neurons recorded from the whisker representation in the somatosensory cortex of urethane anaesthetised rats. The data set (previously published in (Arabzadeh *et al.*, 2003; Arabzadeh *et al.*, 2004)) consists of 24 simultaneously recorded neural clusters, each sampled with a different electrode with a minimal inter-electrode distance of 400 μm. Spike times from each electrode were determined by a voltage threshold set to a value 2.5 times the root mean square voltage. Since it was not possible to sort well-isolated units from each channel, spikes from the same recording channel were considered together as a single neural cluster. It has been estimated that, under these recoding conditions, each cluster captured the spikes of approximately two to five neurons located near the tip of the electrode (see Petersen & Diamond, 2000). Neural activity was recorded in response to stimulation (with a piezoelectric wafer controlled by a voltage generator) consisting of sinusoidal whisker vibrations, each defined by a different value of vibration velocity and delivered for 500 ms (see Arabzadeh *et al.* 2004, for full details). Thirteen different values of vibration velocity were tested, ranging between $Af = 0.15$ mm/s and $Af = 47.7$ mm/s. Each value of vibration velocity was treated as a different stimulus s (there were 13 stimulus classes in total). The number of recorded repetitions for each stimulus (called "trials" in neurophysiology), from which the probability of response at fixed stimulus is determined, varied between a minimum of 200 and a maximum of 1400 across the stimulus classes. We note that this dataset is a convenient one for studying a neu-

ral population under the homogenous-pool assumption. In fact, it was found that
(i) the neurons analyzed here all respond with the same type of profile to velocity
(Arabzadeh *et al.*, 2003), and (ii) when considering pairs of neurons, neglecting the
label of which neuron fired which spikes (which is equivalent to transforming the
response **x** into the response m) did not lead to any significant information loss
(Arabzadeh *et al.*, 2004), which suggests that non-homogeneities are negligible as
far as information transmission is concerned.

We measure the neural responses as follows. We first select a post-stimulus
window in which to measure the neural response. It has been shown (Arabzadeh
et al., 2004) that the majority of the information is transmitted very early post
stimulus onset (typically between 5 and 30 ms). We therefore concentrate on data
taken from these early, highly informative windows. In each trial, the population
response **x** is computed as follows. For each recording channel we set the response
to 1 if at least one spike occurs in the time window, and 0 otherwise. The number m
of neural clusters coincidentally firing is simply computed as the number of clusters
firing at least one spike in the considered window.

We use these data to study the shape of the distribution of the number of clusters
simultaneously firing at fixed stimulus, and the order of neural interactions needed
to describe this distribution. We note that some previous studies (Schneidman *et
al*, 2006) have focused on the overall probability of response to many different
stimuli. However, this has the potential problem that the resulting correlation may
arise both from correlations in the stimulus and in correlations arising from actual
neural interactions, and it is difficult to separate them (Nirenberg & Victor; 2007).
Here, we have decided to consider distributions at fixed stimuli to ensure we only
investigate interactions of neural origin.

We first consider whether the distribution of the number of clusters simultane-
ously firing at fixed stimulus are widespread or concentrated. Distributions condi-
tional to one particular stimulus (velocity = 2.66 mm/s; 1400 trials available) are
shown in Fig. 1, for different values of the size of the post-stimulus window used
to measure the response. For all windows considered, the distribution is clearly
widespread, with no concentration around a single value. Choosing a larger win-
dow, we observe a higher expectation value of the number of neurons firing, but the
distribution remains widespread. These results and trends apply to all 13 stimuli
considered (data not shown).

We next consider whether the observed widespread distributions need high order
interactions among neural activity to be explained. We investigate this issue by
applying the ME algorithms described in Section 3 to the stimulus-conditional
neural response probabilities and considering maximum entropy solutions of various
orders.

Fig. 2 reports a comparison between the real distribution of synchronously fir-
ing clusters in response to stimulus velocity = 2.66 mm/s and the corresponding
maximum entropy models at orders k between 1 and 5. The first and second order
models provide a bell-shaped distribution which are a very poor approximation to
the measured distribution. It is clear that third order is a better approximation
than first and second order, and at fourth and fifth order the maximum entropy
model become difficult to be distinguished from the true distribution. To quantify
the goodness of fit of the maximum entropy models, we used standard χ^2 statistics.
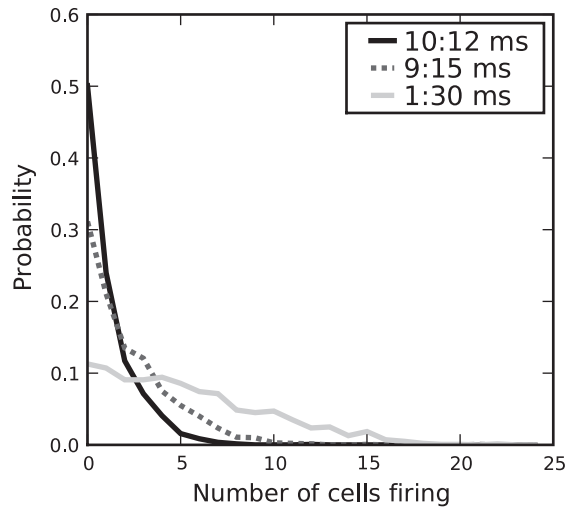The maximum entropy model at order $k = 1, \cdots, 3$ had to be rejected at $p = 0.05$.

Figure 1. Effect of Window on Response Distribution. The distributions obtained depend on the window used to define synchronous activity. Here the distributions in response to stimulus velocity 2.66 mm/s (the best sampled stimulus) from three different time windows relative to stimulus onset are shown.

Models of order 4 and higher were not rejected at $p = 0.05$. The results shown in Fig. 2 are a good description of the typical behavior of the dataset. Considering all probabilities of coincident firing to all the 13 stimuli, 11 stimulus conditional distributions needed at least order 3 interactions to fit the real data (p=0.05), 8 needed at least order 4 (p=0.05), and 6 needed at least order 5 (p=0.05). The only two distributions that could be fit by a model of order two or higher were those with fewer number of trials (those with less statistical power).

6. Effect of Interactions on somatosensory information encoding

Determining the presence of high order interactions suggests that they cannot be neglected in models of information transmission, but it does not tell how much these correlations are important. To quantify this, we next compute the information between the stimulus and the population activity, and we compare it to that derived from the maximum entropy models.

The mutual information between the stimuli and the neural population activity is defined as follows:

$$I(S; X) = H(X) - H(X|S) \tag{5.1}$$

where $H(X)$ and $H(X|S)$ are the response entropy and noise entropy respectively:

$$H(X) = -\sum_{\mathbf{x}} P(\mathbf{x}) \log_2 P(\mathbf{x}) \tag{5.2}$$

$$H(X|S) = -\sum_{\mathbf{x},s} P(s) P(\mathbf{x}|s) \log_2 P(\mathbf{x}|s) \tag{5.3}$$

where in the above $P(\mathbf{x}) = \sum_s P(\mathbf{x}|s) P(s)$. Note that, because of the homogeneity assumption, and because of the data processing inequality, the information about
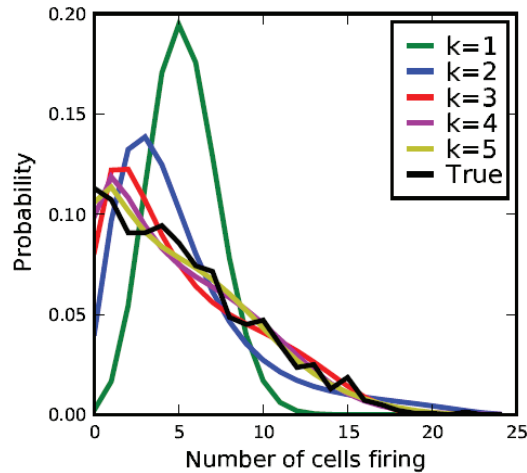
Figure 2. Effect of Interactions on Response Distribution. Here, the distribution conditional on stimulus velocity 2.66 mm/s (the best sampled stimulus) is considered. The maximum entropy solutions are computed for 5 orders ($k = 1 \ldots 5$) and compared to the measured distribution (black line). The windows used to define synchronous firing is 1:30 ms.

the stimuli $I(S; X)$ carried by the population response is equal to the one carried by the rate of coincident firing $I(X; M)$, although as previously discussed the entropies are different.

We investigate the impact of interactions at a given order k by calculating the mutual information that would result from a system exhibiting the probability distributions obtained from the maximum entropy solution, as follows:

$$I^{(k)}(S; X) = H^{(k)}(X) - H^{(k)}(X|S) \tag{5.4}$$

where $H^{(k)}(X)$ and $H^{(k)}(X|S)$ are the response and noise entropies respectively of the k-th order maximum entropy model. These entropies are obtained by replacing $P(X|s)$ and $P(X|s)$ with $P^{(k)}(X|s)$ and $P^{(k)}(X|s)$ in Eqs. (5.2,5.3) where $P^{(k)}(X|s)$ is the maximum entropy solution preserving up to k^{th} order marginals equal to $P(X|s)$ and $P^{(k)}(X) = \sum_s P^{(k)}(X|s)P(s)$. Then

$$I^{(k)}(S; X) = \sum_{m,s} P(s)P^{(k)}(X|s) \log_2 \frac{P^{(k)}(X|s)}{P^{(k)}(X)} \tag{5.5}$$

$I_k(S; X)$ was computed as follows. First, we obtain the homogenous maximum entropy solution, $P^{(k)}(X|s)$, for each order of interest and for each stimulus conditional response. Then, from each of these stimulus-conditional maximum entropy solutions, we simulate data with the same number of trials as available in the experimental data (this is different for each stimulus). These trials are generated using inverse transform sampling. This is done to ensure a fair comparison between the measured data and the generated data; any bias effects should affect both equally. Bias is corrected for using the quadratic extrapolation method (Strong *et al.*, 1998) from the Pyentropy library (Ince *et al.*, 2009). The values obtained are averaged over

1000 repetitions to remove any trial to trial variation from the inverse transform sampling step.
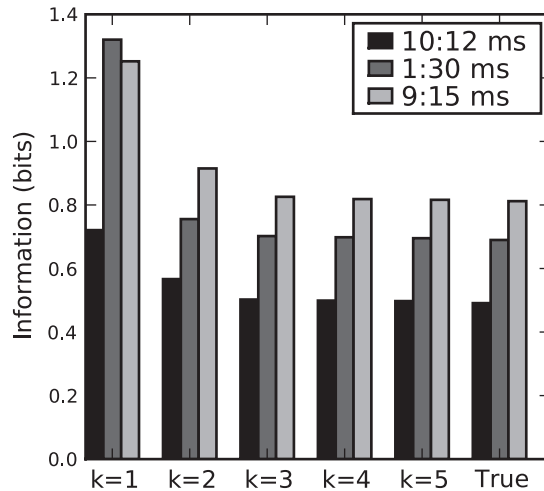

Figure 3. Effect of Interactions on Mutual Information. Here the measured mutual information for three post-stimulus windows are shown, and compared with the mutual information obtained from maximum entropy distributions preserving marginals of up to order $k = 1 \ldots 5$. Interactions of order higher than 3 do not affect the information.

Fig. 3 shows the effect of including higher order interactions on information. Correlations have a limiting rather than an enhancing effect in this neural system. The first and second order maximum entropy models convey significantly higher information than the true system. The third order information is significantly lower than the second order one, suggesting that correlations of order higher than two still have a sizable effect on limiting information. Correlations of order higher than four (though present, see previous section) do not influence information to a significant amount.

The fact that correlations of increasing order limit the information may appear surprising at first glance, but can be explained by considering the variance of the distributions of the rate of coincident firing in Fig. (2). The rate of coincidences from low order maximum entropy solutions have the same mean as the true distribution, but are much more concentrated. As a consequence, the noise entropies of the distributions of coincident firing $H(M|S)$ (obtained from Eq. (5.3) by replacing $P(m|s)$ in lieu of $P(\mathbf{x}|\mathbf{s})$) also increase with the interaction order (Fig. 4). Since, as explained above, the only informative variable in homogenous population activity is the rate of coincident firing m, the information value has to decrease as the interaction order k increases.

Fig. 4 reports the noise and response entropies of the population activity as a function of the interaction order considered. Because of the constrained maximization, the noise entropies have to decrease with the interaction order. However, the noise entropy $H(X)$, which is made up mixing all stimulus conditional responses, is not constrained to necessarily decrease as fast as $H(X|S)$ with the interaction

order (Schultz & Panzeri, 2001). In fact, $H(X)$ decreases more quickly with k than $H(X|S)$ does (Fig. 4), thus leading to an overall information decrease with increase of order k.
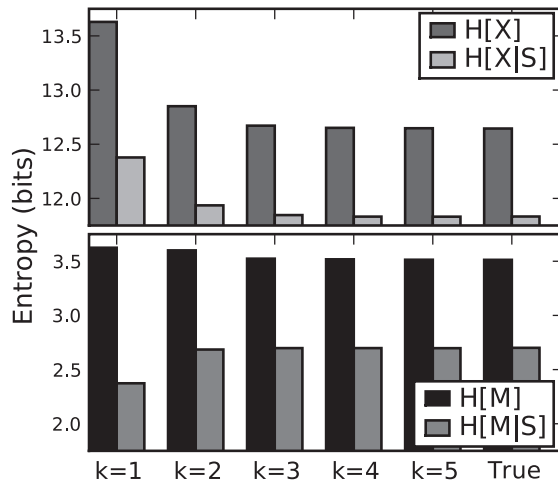

Figure 4. Effect of Interactions on Entropies. Here we show the conditional and unconditional entropies of the measured distribution (True) and maximum entropy solutions preserving marginals of up to order $k = 1\ldots 5$ for the maximally informative window *9:15* ms. Both the entropy of coincident rate and the entropy of the full population response are shown. The entropies over population response decrease with increasing order, as required by the maximum entropy condition, but this is not true of the entropies of the rate of coincident firing. However, the information transmitted (difference between the two bars in each plot) is the same for both.

It is interesting that the mutual information of the system is already well approximated by models containing interactions of up to order 3. Interactions of order higher than 3, though statistically significant, do not appear to play a qualitatively important role in information transmission. This is a significant simplification since it greatly reduces the parameters required to describe the system. While it is still challenging to sample up to third order marginals it is a much more tractable problem than the case where all orders of interaction must be accurately determined.

6. Discussion

Here, we have considered, to our knowledge for the first time, how an homegenous-pool model containing interactions of arbitrary order (Bohte *et al.*, 2000; Amari *et al.* 2003) fits real distributions of the rate of coincident firing in real *in vivo* neural networks. We found that, when considering stimulus-conditional distributions of the rate of simultaneous discharge in populations including tens of recorded neural clusters, interactions of order higher than two are typically needed to describe the distributions. Thus, interactions of order two may not always be sufficient to describe the correlational structure of neural activity, as recently reported (Schneidman *et al.*, 2006; Shlens *et al.*, 2006; Tang *et al.*, 2008). In addition to studying

the effects of interactions on the mutual information, it would also be interesting to investigate the θ-coordinate scaling properties as proposed in (Amari *et al.*, 2003). However, the currently available experimental data is insufficient, since it does not contain enough simultaneously recorded channels to approach the large N regime of the theory.

In this paper we have also reported what constitutes, to our knowledge, the first calculation of the impact of higher order firing on the mutual information about sensory stimuli carried by a neural population. Previous studies mostly concentrated on the effect of interaction on response entropy. Since typically mutual information is smaller compared to both the response and the noise entropy, an impact that may be proportionally small for entropy may be proportionally much longer when considering information. In the system considered here, we found that correlations decreased the information, and the decrease in information became larger as the interaction order grew, and saturated at order 3. This suggests that, when evaluating the computational capacity of cortical population in sensory areas, it may be necessary sometimes to take into account correlations of order higher than two. Thus, it is particularly important to be able to extend analytical models of the effect of correlation on information to order higher than two, and to be able to compute their scaling in their thermodynamic limit. We believe that this will become an important topic for future theoretical research on the encoding capacity of neural networks.

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