An Information-Theoretic Approach to Neural spike correlations

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Abstract We have applied an information theoretic approach to gain insights of the role of spike correlations in the neuronal code. We use a modified version of the information components breakdown to quantify the contribution of individual members of the population, the interaction between them, and the overall information encoded by the ensemble of neurons making an especial emphasis of the separation between contributions due to the noise and signal spike correlations. We present examples of applications of this formalism to simultaneous recordings of multiple spike trains.

1 Introduction

At the beginning of the twentieth century (Adrian and Zotterman, 1926) using the afferent nerve of stretch receptor in the frog muscle, showed that it was possible by amplification to record the impulse in single nerve fibbers. They summarized their results in this single sentence: "The impulses set up by a single end-organ occur with a regular rhythm at a frequency which increases with the load on the muscle and decreases with the length of time for which the load has been applied". Ever since Adrian and Zotterman observed that the firing rate of peripheral touch receptors coded for the pressure applied to a patch of skin, neuroscientists have been trying to understand the neural code.

However, understanding brain functions requires interdisciplinary approaches involving many levels of study: from the molecular level through the cellular level

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(individual neurons), to the level of relatively small assemblies of neurons (for example cortical columns); to the case of larger subsystems as the one which subserves visual perception, and up to the level of large systems including the cerebral cortex, the cerebellum, and to nervous system as a whole. Neuroscience encompasses approaches ranging from molecular and cellular studies to human psychophysics and psychology. Moreover, theoretical analysis of physiological data and computational modeling are important tools for characterizing what nervous systems do, determining how they function, and understanding why they operate in particular ways.

Unfortunately, it is extremely difficult to understand exactly how sensory information is processed in the mammalian brain. For example, the influx of sensory information to a single mammalian superior retina is detected by an array of millions of receptors, each capable of detecting the difference between hundreds of gray levels. They have integration times which allow them to detect new signals in just a few seconds. These inputs are then processed by hundreds of millions of other neurons, and many of them interact with each other in complex ways. Moreover, depending on stimulus conditions a different sort of inputs is generated which will eventually modify these interactions dynamically. With this huge level of complexity, the experimental tools which have been available during the last thirty years were insufficient to account for all the involved variables.

One of the main experimental challenges in neuroscience during the last thirty years was to demonstrate that distributed neural populations in the visual cortex process information in a cooperative way. The visual cortex is composed of a large number of areas, which contain neurons that are tuned to different visual features. Temporally correlated activity of individual neuronal pairs within the visual cortex has been investigated in many laboratories since the early 1980s (Toyama et al., 1981a; Michalski et al., 1983; Toyama et al., 1981b; Ts'o et al., 1986; Aiple and Krueger, 1998; Ts'o and Gilbert, 1988; Gochin et al., 1991; Hata and Tamura, n.d.; Alonso and Martinez, 1998; Molotchnikoff and Shumikhina, 1998), most often with a motivation to reveal structural coupling between cells. This approach to functional anatomy had been methodologically and conceptually outlined by (Perkel et al., 1967; Gerstein and Perkel, 1969; Moore et al., 1970; Kirkwood, 1979; Aertsen et al., 1989; Surmier and Weinberg, 1985), and successfully applied to the invertebrate nervous system (Bryant et al., 1973). The results of these different studies showed the presence of temporally precise synchronization within the cat and macaque visual cortex. But, these correlations occurred between cells showing the same feature preference. Because the peaks in the correlograms were centered around zero the obtained correlations were attributed to common inputs and no attempts were made at this stage to determine whether response synchronization depend on the stimulus configuration.

Neurons in cortex receive 3,000-10,000 synaptic inputs, 85 % of which are excitatory. Nearly half of the excitatory input to any one neuron comes from nearby neurons that fall within a cylinder of 100-200 μ m radius, arranged as a column, sometimes termed a mini-column (Desimone, 1991; Andersen, 1995; Churchland et al., 1994; Cobb et al., 1995). This suggests that cortical neurons receive abundant excitatory input and are embedded in a network of highly convergent signals.

The networks have a recurrent nature, it is likely therefore that those most excitatory neurons receive similar inputs and emits spikes under similar conditions. This means that the conditions that lead to a response of any of one neuron in minicolumn are likely to involve considerable activity from a large number of its inputs and its outputs. It is therefore reasonable to expect that many spikes inputs will arrive in synchrony within a very small time window.

To investigate the role of temporal correlated neuronal activity is a key element for the understanding of the neuronal coding. To get a better understanding of the role of correlations can have widespread implications, not only for our basic understanding of how the brain operates, but also in our understanding of neuronal dysfunctions (Uhlhaas and Singer, 2006).

However, the matter of how the coding of sensory information is affected by spike correlations across neurons has been fraught with dissension, and the debate has become polarized into two different postures that co-exist in the neuroscientific community. One of the postures, supported by many authors (Eckhorn et al., 1998; Gray and Singer, 1989; Gray et al., 1989; Meister et al., 1995; Vaadia et al., 1995; De Charms and Merzenich, 1996; Dan and Reid, 1998; Steinmetz et al., 2000) is that correlations are important in the coding of sensory information, whereas others have proposed that they are not important (Nirenberg et al., 2001; Oram, 2001; Petersen et al., n.d.; Levine et al., 2002; Panzeri, Pola, Petroni, Young and Peterson, 2002; Panzeri, Golledge, Zheng, Pola, Blanche, Tovee and Young, 2002; Averbeck et al., 2003; Averbeck and Lee, 2003; Averbeck and Lee, 2004; Golledge et al., 2003).

This dissension can be traced to different methods used to asses the role of synchronized spike firing. For instance, one of the most used methods consisted in looking for stimulus-dependent changes in cross-correlograms (Eckhorn et al., 1998; Gray and Singer, 1989; Gray et al., 1989; Vaadia et al., 1995; De Charms and Merzenich, 1996). However, the firing rate can alter the shape of cross-correlograms making it difficult to separate information carried by firing rates from information carried by correlations. Moreover, cross-correlograms account only for near synchronous spikes. This is, they do not account for correlations which occur on a longer time scales and among patterns of spikes.

Information Theory provides us with a measure of the uncertainty in a message. It was invented as a general framework for quantifying the ability of a coding scheme or a communication channel (such an optic nerve) to convey information (Shannon, 1948). It is assumed that the code involves a number of symbols (such as different neuronal responses), and that the coding and transmission process are stochastic and noisy. Communication channels, if they are noisy, have only limited capacities to convey information. The techniques of information theory are used to evaluate these limits and find coding schemes that saturate them. Moreover, information theory allows us to address how much the neuronal responses tell us about the stimulus. We can use them to ask what forms of neuronal response are optimal for conveying information about the neuronal stimuli. Therefore many brain structures can be considered as communication channels, and an appropriate mathematical framework is the Information Theory.

2 Entropy estimators

In this section we will review some of the basic problems of entropy and mutual information estimations for discrete variables and give a brief classification of different approaches to the problem.

It is well known that the naive or "plugin" estimator of entropy tends to underestimate it (it is biased). This is can be understood in the framework of the Jensen inequality (Cover and Thomas, 1991). The entropy is a concave function and therefore a "plugin" estimator of entropy tends to underestimate the real value of the entropy (a rigorous proof of this statement can be found in (Paninski, 2003). The usual approach has been to attempt to avoid this by the use of a perturbative expansion in the asymptotic regime (Panzeri and Treves, 1996). An alternative idea, that of calculating entropy by counting coincidences, was proposed a long time ago by Ma for physical systems in the micro-canonical ensemble, where a uniform distribution of entropy corresponds to states of fixed energy (Ma 1981). In a neuroscience context, this would correspond to the assumption that the probability distribution of response words at a fixed spike count is close to uniform (Strong et al., 1998; Schultz and Panzeri, 2001). The Bayesian approach proposed by Nemenman, Shafee and Bialek (Nemenman et al., 2002), building upon ideas formulated by (Wolpert and Wolf, n.d.) and (Samengo, 2002), extends this idea to arbitrarily complex distributions. The goal of the NSB method is to construct a Bayesian prior which generates a nearly uniform distribution of entropies in order to correct sample size dependent bias at its source.

In the following we are going to review the basic ideas of the NSB entropy estimator method (Nemenman et al., 2004), and we will compare the effectiveness of NSB in comparison with the computation of the entropy via the naive "plugin" approach, and by using a sophisticated analytical method for correcting bias (Panzeri and Treves, 1996).

Consider the problem of estimating the Shannon entropy for a given probability distribution $\mathbf{p} = \{p_i\}$,

$$H = -\sum_{i=1}^{K} p_i \log_2 p_i \tag{1}$$

where the index i runs over K possibilities. For instance, $\mathbf{p}$ might be the distribution of spike counts observed to be fired by a neuron – in which case i would represent "number of spikes + 1" (as zero spikes fired is also a possible response). Consider N samples (trials) which were obtained from a given experiment, where each possibility i occurred n_i times: if N is much bigger than K we can approximate $p_i \approx f_i = n_i/N$, and therefore the entropy can be expressed in terms of the observed frequencies as

$$H_{naive} = -\sum_{i=1}^{K} f_i \log f_i \tag{2}$$

The problem is that this "plugin" approach tends to underestimate the entropy. Neurophysiologic experiments can only convey a finite number of trials, and therefore the true stimulus-response probabilities cannot be estimated exactly. The estimated probabilities fluctuate around their true values. Several attempts to solve this problem were made by (Carlton, 1969), who made asymptotic bias corrections by adding a term of order *O(K/N)*. This approach was developed further by (Panzeri and Treves, 1996), and amounts to (in brief)

$$H = H_{naive} + Bias[H(R)] \tag{3}$$

where

$$Bias[H(R)] \approx -\frac{1}{2N ln2} \sum_s \hat{R}_s \tag{4}$$

and $\hat{R}_s$ denotes the number of relevant bins for for a trial with stimulus *s*, i.e. the response bins in which the occupancy probability $p(i|s)$ (at given s) is non-zero. Note that if a bin is observed never to be occupied, it is ambiguous whether that is because it has a true zero occupancy probability, or because responses simply have not been observed for long enough. Choice of $\hat{R}_s$ is a subtle issue, and is to some extent dependent upon data characteristics. (Panzeri and Treves, 1996) made use of a Bayesian prior for the number of relevant bins, and iteratively re-estimated it. This procedure has been found to be effective for a number of types of single-unit electrophysiology data (e.g. (Panzeri and Schultz, 2001; Rust et al., 2002)), but after much detailed analysis, we found its performance to be inadequate for the analysis of many of the pairs in the V1 dataset, despite the relatively large number of trials available (480-3200) compared to many other information theoretic analyses in the literature. This is, an adequate sampling was obtained with NSB at as low as 100 trials, but this was not the case with other entropy estimators.

Several approaches for estimating entropies without using such an asymptotic expansion approach have recently been presented (Nemenman et al., 2004; Paninski, 2003). We will follow the approach of Nemenman et al.

Recall our examination of the probability distribution **p** from equation (2). Bayes' rule tells us that we can express the posterior probability of **p** ($\equiv \{p_i\}$, $i = 1..K$ discrete random variable) , given that we have just observed *i* to have occurred n_i times.

$$P(p|n_i) = \frac{P(n_i|p)P(p)}{P(n_i)} \tag{5}$$

Note that the number of times we observe each response value i to occur must add up to the total number of experimental trials N.

$$\sum_{i=1}^{K} n_i = N \tag{6}$$

In equation (5), the "prior" distribution is $P(\mathbf{p})$ – in principle, we could choose a prior such that our estimator of the entropy of $P(\mathbf{p})$ does not depend upon the number of trials. This is obviously a desirable quality! To do this, we can express $P(\mathbf{p})$ in terms of the Dirichlet family of priors (Nemenman et al., 2004). This should allow us to construct a prior which does not depend on inverse powers of N (which even the naive approximation does implicitly, as $f_i = n_i/N$). The Dirichlet family are characterised by a parameter β; they can be written as

$$P_\beta(p) = \frac{1}{Z} \delta(1 - \sum_{i=1}^{K} p_i) \prod_{i=1}^{K} p_i^{\beta-1} \tag{7}$$

where

$$Z = \frac{\Gamma^K(\beta)}{\Gamma(K\beta)} \tag{8}$$

δ and Z are functions which enforce the normalization of $\mathbf{p}$ and P_β respectively (δ being the Dirac delta function, and Γ stands for Eulers Γ function). Maximum likelihood estimation corresponds to Bayesian estimation with this prior in the limit $\beta \to 0$, while a uniform prior is implemented by $\beta = 1$. (Nemenman et al., 2002) observed that fixing a particular value of β (and thus fixing the prior) specifies the entropy almost exactly. For an "incorrect" prior, the estimate of entropy is thus dominated by the prior, rather than determined by our actual knowledge – that is to say, it is biased.

Ideally, we would like to compute the whole *a priori* distribution of entropies

$$P_\beta(H) = \int dp_1 dp_2 ... dp_K P_\beta(\{p_i\}) \delta(H + \sum_{i=1}^{K} p_i \log_2 p_i) \tag{9}$$

But this is quite difficult to achieve. In order to get an entropy estimate with small bias one could simply fix a flat prior distribution of entropy $P(H)$. One way of doing so is by defining

$$P(H) = 1 = \int \delta(H - \xi) d\xi \tag{10}$$

where ξ is the expected entropy. If we could find a family of priors $P_\beta(\mathbf{p})$ which result in δ functions over H, and if by changing β we move the peak across the

whole range of entropies uniformly, then we will effectively be choosing the proper prior for each entropy. We will thus come close to the objective of removing bias at its source. Because the entropy of distributions chosen for P_β is sharply defined and monotonically dependent on the parameter β we can effect this goal by averaging over β. The main idea of the NSB approach is thus to construct a prior

$$P_\beta(p) = \frac{1}{Z}\delta(1 - \sum_{i=1}^{K} p_i)\prod_{i=1}^{K} p_i^{\beta-1}\frac{d\xi(\beta)}{d\beta}P(\beta) \tag{11}$$

which will perform this task even when N is small. In this equation Z is again a normalizing coefficient and $\frac{d\xi(\beta)}{d\beta}$ ensures the uniformity for *a priori* expected entropy ξ.

This Dirichlet priors allow all the K dimensional integrals to be calculated analytically (see (Wolpert and Wolf, n.d.), giving for the moments of the entropy

$$(H^{NSB})^m = \frac{\int d\xi\rho(\xi,n)\langle H^m(n)\rangle_{\beta(\xi)}}{\int d\xi\rho(\xi,n)} \tag{12}$$

where $\mathbf{n}=\{n_i\}$, and m=1,2 correspond to the entropy and its second moment. $\langle H^m[n_i]\rangle_{\beta(\xi)}$ is the expectation value of the mth entropy moment at a fixed β (Wolpert and Wolf, n.d.) and the posterior density is a function of the proposed Dirichlet prior,

$$\rho(\xi|n) = P_\beta(\xi)\frac{\Gamma(\kappa(\xi))}{\Gamma(\beta(\xi))}\prod_{i=1}^{K}\frac{\Gamma(n_i+\beta(\xi))}{\Gamma(\beta(\xi))} \tag{13}$$

Summarizing, the main idea of NSB is to construct a Bayesian prior, which generates a nearly uniform distribution of entropies in order to avoid bias at its origin. These results were obtained by (Nemenman et al., 2002; Nemenman et al., 2004); we have tried here to give, in as simplistic terms as possible, an explanation of how the method works. We will now illustrate the performance of the method with an example.

2.1 Example: Information available for a single pair of neurons

In order to test the effectiveness of the entropy estimator developed by (Nemenman et al., 2004), we performed calculations of the total mutual information conveyed by a single pair of cells in V1 (Kohn and Smith, 2005) using the naive estimator, using the Panzeri-Treves bias correction, and using the NSB method. Figure 1 shows the total information estimated through these different approaches. The ensemble (pair) mutual information was calculated using different subsets of the total available

number of trials, which *in this case* was sufficient for all methods to converge to the same asymptote, which we can consider to be the true information. The results speak for themselves.
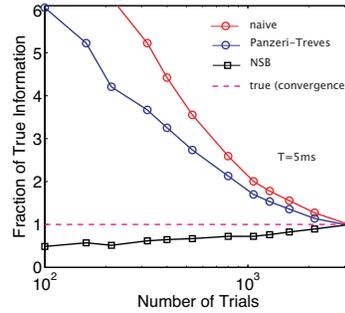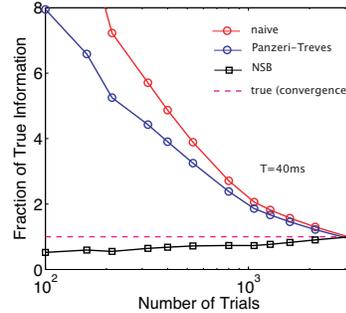
Fig. 1 Relative performance of several information estimators. Two different time windows were chosen for counting spikes: **A** 5ms, resulting in cardinality $K = 10$ from the ensemble responses. **B** 40 ms, cardinality $K = 76$.

The NSB approach was the only one we found to be adequate across the entire dataset, despite the relatively large number of trials available (480-3200) compared to many other information theoretic analysis in the literature. Note that this was a particularly (although not entirely unusual) hard to sample pair of cells; for some other pairs, adequate sampling was obtained by NSB at as low as 100 trials.

2.2 Numerical Implementation

It can be found online two different implementations of the NSB method available from the authors http://nsb-entropy.sourceforge.net/. We have converted the Octave

code to a MatLab compatible version. The source code of implementation are in C++ and MatLab/Octave.

NSB requires a substantial amount of numerical integration and function inversion. The Matlab version is pretty basic in its functionality, works cross-platform, but this version has the inability of MatLab to index discrete structures that can exist in a space with cardinality of more than 2^{32}. The C++ code is faster.

3 The role of correlations in the neural code

In this work, we review how to use an information theoretic approach to investigate the neuronal code. We discuss how to quantify the information carried by spike correlations in the neural population, and we present examples of applications of this formalism to simultaneous recordings of multiple spike trains.

3.0.1 Methods

To characterize the neuronal responses by a given stimuli is indeed very difficult because of the complexity and variability of these responses. Neurons typically respond by producing complex spike sequences that reflect both the intrinsic dynamics of the neuron and the temporal characteristics of the stimulus. Isolating features of the response that encode changes in the stimulus can be difficult, especially if the time scale for these changes is of the same order as the average interval between spikes. Neuronal responses can vary from trial to trial even when the same stimulus is presented repeatedly. There are many potential sources of this variability including variable levels of arousal and attention, randomness associated with various biophysical processes that affect neuronal firing, and the effects of other cognitive processes taking place during a trial.

The complexity and trial-to-trial variability of action potential sequences make it unlikely that we can describe and predict the timing of each spike deterministically. Instead, a complete description of the stochastic relationship between a stimulus and a response would require us to know the probabilities corresponding to every sequence of spikes that can be evoked by the stimulus. That is, the neural responses and their relationship to the stimuli are completely characterized by the probability distribution of spikes times as function of the stimulus. The independent-spike code corresponds to the case in which the generation of each spike is independent of all other spikes in the train. In contrast, if the individual spikes do not encode independently of each other, we call the code a correlation code, because correlations between spikes times may carry additional information. In fact, information is likely to be carried by both individual spikes and through correlations, and some arbitrary dividing line must be established to characterize the code.

Part of the difficulty in understanding population coding is that neurons are noisy and the same pattern of activity never occur twice, even if the same stimulus is pre-

sented. Because of this noise, population coding is necessarily probabilistic. One of the prevailing view of neural coding is that the meaningful signal is contained in the mean rate of the action potential discharges of a neuron, and rate variability is just noise. This noise may be filtered out by averaging across time or neuronal populations, rate coding can performs robustly in the presence of noise, but it has limited information capacity. This is, noise in the brain is correlated and it is essential we gain a thorough understanding of the correlational structure in the brain and its possible impact in the population code. An alternative view of the neural code is summarized by the term temporal coding; the notion that the timing of individual spikes also carries relevant information. In principle, selective temporal mechanisms could exploit the high intrinsic precision of cortical neurons to increase the efficiency of neural coding.

How to account for the entire complexity levels present in the brain signals just by using a single theoretical approach ? Information theory is the most rigorous way to quantify neural code reliability and constitutes an aspect of probability theory which allows us to quantify the information transmitted by communication channels (Shannon, 1948). One possible application could be to quantify how much information neuronal activity carry about external sensory stimuli. More importantly, the exact breakdown of Information into its coding mechanisms allows a precise quantification of all the modalities with which correlations contribute to the neural code.
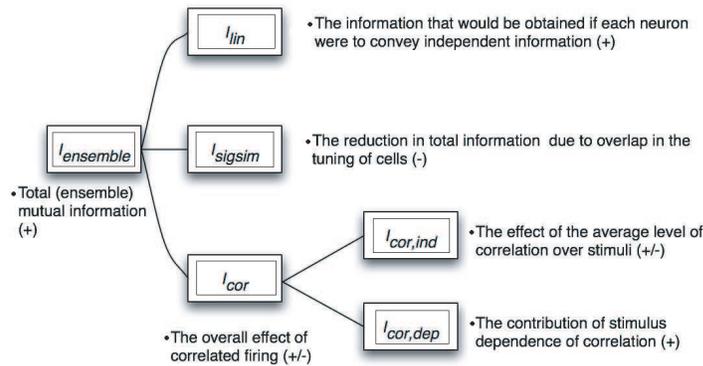
Fig. 2 Information component breakdown. The ensemble mutual information can be broken down into a linear component, the reduction of information due to the redundancy caused by overlap in tuning curves, and the contribution of correlated firing (I_{cor}). The correlation term can be further broken down to separate out the effect of the average level of correlation over all stimuli, and the stimulus-dependence of correlation – the latter term captures any effects due to coding by explicit modulation of correlation/synchronization.

Shannon's Information Theory formalizes the relationship between events, such as stimulus and response events, strictly based on their probabilities of occurrence

(e.g., $P(s_i|r_j)$, the probability that stimulus s_i occurred given the response r_j). Information Theory allows us to address how much the neuronal responses tell us about the stimulus independently of any mechanism or model.

Information theory tells us how much information about a set of stimuli is encoded in a set of responses, which is a measure of how accurately we can know what stimulus was presented, given the response. This measure can also be defined as the reduction in uncertainty about which stimulus was presented before and after analyzing the response.

In this section we describe how we calculate the Shannon information transmitted by neuronal population activity (and a number of related quantities). Shannon mutual information quantifies the extent to which the responses are dependent upon the stimuli – it is a distance-like measure (the Kullback-Leibler divergence) between two probability distributions: the joint probability of responses and stimuli, $P(\mathbf{r},\mathbf{s})$, and joint probability distribution that would apply if responses did not depend at all upon stimuli, $P(\mathbf{r})P(s)$. This dependence between responses and stimuli may take a number of forms – firing rate dependence, pairwise correlation dependence, etc. Information component breakdown methods (Figure 2) allow us to quantify the effect of such dependencies upon the mutual information and thus assess the different ways in which the correlations contribute to the neural code. If synergistic or redundant interactions between cells are observed, the information components may reveal the mechanisms from which they arise.

The technical approach we adopt is a modification of a previously developed technique (Panzeri and Schultz, 2001; Schultz and Panzeri, 2001; Panzeri et al., 1999) in which a Taylor series expansion was used to break the Shannon information into its components. Pola et al (2003)(Pola et al., 2003) generalised this approach by substituting correlation functions with probability functions, resulting in an exact information component breakdown. One disadvantage to the Pola approach is that the correlation components cannot be explicitly written in terms of entropies of probablity distributions. While we do not see this as giving rise to problems of interpretation (but see Schneidman et al 2003), it does mean that advanced methods for entropy estimation cannot be used. Thus we have rewritten the correlational components as *approximate* entropies (i.e. an entropies plus additional terms which are very small and relatively immune to bias), allowing us to use a recently developed technique for minimizing the bias associated with estimating entropy from a limited number of experimental samples (Nemenman et al., 2004). By using a Bayesian prior to generate a nearly uniform distribution of entropies, we thus correct for sample size dependent bias at its source and avoid potential artefacts that may occur when sampling is insufficient, as is typically the case in neurophysiological experiments.

We consider a time period of duration T unit time bins in which the activity of a given pair of cells is observed. The neural population response will be denoted by $\mathbf{r}$ (drawn from a response space R*)* and a sensory stimulus from a given stimulus set S will be denoted by s. The mutual information transmitted by the population response about the whole set of stimuli (Shannon, 1948; Cover and Thomas, 1991) is written as

$$I(R;S) = H(R) - H(R|S),\tag{14}$$

where $H(R)$ and $H(R|S)$ are the total response entropy and the noise entropy respectively. They are defined as:

$$H(R) = -\sum_{\mathbf{r}\in R} P(\mathbf{r}) \log_2 P(\mathbf{r}),\tag{15}$$

$$H(R|S) = -\sum_{s\in S} P(s) \sum_{r\in R} P(\mathbf{r}|s) \log_2 P(\mathbf{r}|s),\tag{16}$$

where $P(r|s)$ is the probability of observing a given ensemble response vector r conditional upon the occurrence of stimulus s, and $P(r)$ is the average of $P(r|s)$ over all stimuli.

In order to understand the meaning of correlation one must define the probability of getting independent population responses as:

$$P_{ind}(\mathbf{r}|s) = \prod_{c=1}^{C} \prod_{t=1}^{T} P(r_{ct}|s),\tag{17}$$

and

$$P_{ind}(\mathbf{r}) = \langle P_{ind}(\mathbf{r}|s) \rangle_s,\tag{18}$$

where c is the label for each cell (up to $C=2$ cells in the pair for the analysis presented here, although the formalism is quite general in this respect),t indexes the time bin up to a maximum value of L corresponding to duration$T$, and the stimulus average $\langle x \rangle_s = \sum_{s=1}^{S} P(s)x$. The presence of noise correlation (correlation in the response variability for a fixed stimulus) or signal correlation (correlation in the tuning of, or signal conveyed by response variables) is indicated by $P_{ind}(\mathbf{r}|s) \neq P(\mathbf{r}|s)$ and $P(\mathbf{r}) \neq P_{ind}(\mathbf{r})$, respectively. Moreover, $P(s|r)$ is the true distribution of stimuli given responses and $P_{ind}(s|\mathbf{r})$ is the distribution one would derive in absence of knowledge of correlations. In practice, we obtained $P_{ind}(\mathbf{r}|s)$ numerically by multiplying the marginal probability distributions as apparent from 17.

The information component breakdown method allows us to write the total mutual information into a sum of components which are related to the different decoding mechanism (Panzeri and Schultz, 2001; Pola et al., 2003)

$$I(R;S) = I_{lin} + I_{sig-sim} + I_{cor}\tag{19}$$

The first term of the information breakdown, I_{lin}, gives the total amount of information which would be conveyed if all the cells were independent:

$$I_{lin} = \sum_{c=1}^{C}\sum_{t=1}^{T}[H(R_{ct})-H(R_{ct}|S)] \tag{20}$$

where

$$H(R_{ct}|S) = -\sum_{s\in S}P(s)\sum_{r_{ct}}P(r_{ct}|s)\log_2 P(r_{ct}|s), \tag{21}$$

and $H(R_{ct})$ is the averaged value across all the stimuli.

The signal similarity term $I_{sig-sim}$ quantifies the information loss arising from redundancy due to overlap in the tuning curves pertaining to response (cell,time) bins r_{ct} ("redundancy due to signal correlations")

$$I_{sig-sim} = H_{ind}(R) - \sum_{c=1}^{C}\sum_{t=1}^{T}H(R_{ct}), \tag{22}$$

where

$$H_{ind}(R) = -\sum_{\mathbf{r}}P_{ind}(\mathbf{r})\log_2 P_{ind}(\mathbf{r}), \tag{23}$$

The third term, I_{cor}, quantifies the total amount of information due to the correlated activity on the overall neural coding:

$$I_{cor} = I(R;S) - H_{ind}(R) + \sum_{c=1}^{C}\sum_{t=1}^{T}H(R_{ct}|S). \tag{24}$$

This is, I_{cor} quantifies whether the presence "correlation" increase or decrease the information available in the neural responses.

It is important to point out that correlations in response profiles of individual signal across different stimuli are called "signal correlation" because they are entirely attributable to stimulus selectivity. On the other hand, correlations which are manifested as covariation of the trial-by-trial fluctuation around the mean response to the stimulus are named "noise correlations". These covariations are observed at fixed stimulus, and they are not attributable to the stimulus.

So far, it is apparent that all of the terms can be written in terms of entropies of particular distributions. However, this correlation term can be further resolved into two components, a stimulus independent component $I_{cor-ind}$ and a stimulus

dependent component $I_{cor-dep}$. This last term in the (Pola et al., 2003) formalism is calculated as

$$I_{cor-dep} = I(R;S) - \chi + \sum_c H(R_c|S), \tag{25}$$

where

$$\chi = -\sum_{\mathbf{r}} P(\mathbf{r}) \log_2 P_{ind}(\mathbf{r}), \tag{26}$$

That is, the stimulus dependent correlation component is not made up entirely of entropies, and thus advanced entropy estimation techniques such as NSB cannot be applied. Moreover, χ can be substantially biased, which renders its calculation by previously available procedures difficult for all except very low-dimensional problems.

Formally speaking, the stimulus dependent correlation component can be defined as the Kullback-Leiber divergence between $P(s|\mathbf{r})$ and $P_{ind}(s|\mathbf{r})$, (Nirenberg et al., 2001; Latham and Nirenberg, 2005) – conceptually characterized by Nirenberg et al as the effect of correlations upon the decoding of stimuli:

$$I_{cor-dep} = D\left(P(s|\mathbf{r}) \| P_{ind}(s|\mathbf{r})\right) \equiv \sum_{\mathbf{r}} P(\mathbf{r}) \sum_s P(s|\mathbf{r}) \log_2 \frac{P(s|\mathbf{r})}{P_{ind}(s|\mathbf{r})} \tag{27}$$

In the following we rewrite the correlation stimulus dependent component from "first principles" using the Kullback-Leibler, for the case in which only pairwise correlations between neurons are considered. We note that this formalism can be easily extended to a larger number of cells.

$$I_{cor-dep} = D\left(P(s|r_1 r_2) \| P_{ind}(s|r_1 r_2)\right) \equiv \sum_{r_1 r_2} \sum_s P(s)P(r_1 r_2|s) \log_2 \frac{P(r_1 r_2|s)}{P_{ind}(r_1 r_2|s)} \tag{28}$$

$$\sum_{r_1 r_2} P(r_1 r_2) \log_2 \frac{P(r_1 r_2)}{P_{ind}(r_1 r_2)}$$

where

$$P_{ind}(r_1 r_2) = \sum_s P(s)P(r_1|s)P(r_2|s) \tag{29}$$

and

$$P(r_1 r_2) = \sum_s P(s)P(r_1 r_2|s) \tag{30}$$

The second term in the Kullback-Leibler distance, $D_\Delta = \sum_{r_1 r_2} P(r_1 r_2) \log_2 \frac{P(r_1 r_2)}{P_{ind}(r_1 r_2)}$, does not change if we multiply and divide by exactly the same factor inside the logarithm.

$$D_\Delta = -\sum_{r_1 r_2} P(r_1 r_2) \log_2 \left(\frac{P(r_1 r_2) \langle P(r_1|s) \rangle_s \langle P(r_2|s) \rangle_s}{\langle P(r_1|s) P(r_2|s) \rangle_s \langle P(r_1|s) \rangle_s \langle P(r_2|s) \rangle_s} \right), \qquad (31)$$

This is equivalent to saying

$$D_\Delta = \sum_{r_1 r_2} P(r_1 r_2) \log_2 \frac{P(r_1 r_2)}{\langle P(r_1|s) \rangle_s \langle P(r_2|s) \rangle_s} - \Delta = I(r_1; r_2) - \Delta \qquad (32)$$

where $\Delta = \sum_{r_1 r_2} P(r_1 r_2) \log_2 \beta$
and,

$$\beta = \frac{\langle P(r_1|s) \rangle_s \langle P(r_2|s) \rangle_s}{\langle P(r_1|s) P(r_2|s) \rangle_s}, \qquad (33)$$

the correlation stimulus dependent component can be rewritten as

$$I_{cor-dep} = \sum_{r_1 r_2} \sum_s P(s) P(r_1 r_2|s) \log_2 \frac{P(r_1 r_2|s)}{P_{ind}(r_1 r_2|s)} - \qquad (34)$$

$$\sum_{r_1 r_2} P(r_1 r_2) \log_2 \frac{P(r_1 r_2)}{\langle P(r_1|s) \rangle_s \langle P(r_1|s) \rangle_s} - \Delta,$$

The stimulus dependent correlation component has thus been expressed in terms of entropy quantities with the addition of a single term Δ; the NSB estimation method can be applied to these quantities with the exception of Δ. The remaining non-entropy term (Δ) is essentially the stimulus-averaged response multiplied by a logarithmic function of the coefficient β summed over the whole space of responses. We are summing therefore in the space of responses quantities which have been averaged over the stimuli, and it is reasonable to expect a very low bias contribution from this term. Moreover, since β is the product of the stimulus-averaged response from each cell divided by the stimulus unconditional independent responses, it is reasonable to expect that it will always be close to one and therefore Δ will be close to zero. In practice, we included Δ in our calculations (without bias correction); the magnitude of Δ was always observed to be small.

Figure 3 shows an histogram of the ratio between the true value of I_{cordep} and that obtained by setting $\Delta=0$. We conclude from the histogram that the contribution from Δ will be reasonably small. In practice, we included Δ in our calculations (without bias correction).
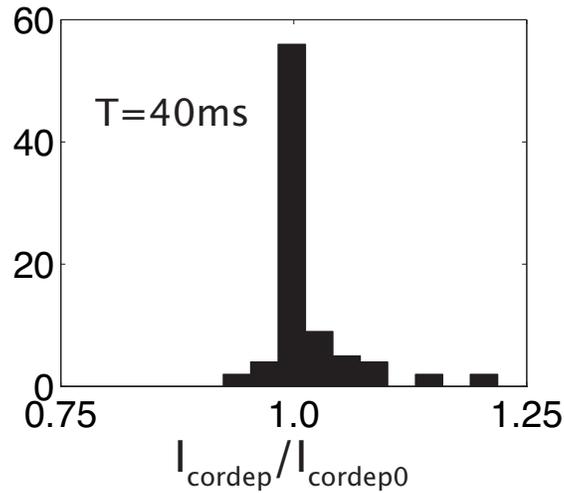
Fig. 3 The effect of Δ (at $T = 40$ ms for 102 pairs of neurons). $I_{cordep0}$ correspond to $\Delta = 0$.

Having expressed all of the quantities necessary to perform the information component analysis in terms of entropies of particular (in some cases conditional) distributions, these entropies are computed by inserting the respective distributions into the NSB entropy estimation routine. We found that, for our dataset, this procedure resulted in substantially better estimation performance than we were able to achieve with techniques that we have used previously (Panzeri and Treves, 1996). In addition, the NSB approach provides a convenient error estimate for the entropies, which can be propagated into error estimates for the information quantities. An alternative method to estimate $I_{cor-dep}$ has been also recently developed by (Montemurro et al., n.d.).

We have expressed all information quantities in total information terms, measured in bits, as opposed to rates measured in bits/sec. In the context of the present study we believe that this leads to a clearer interpretation; a discussion of the application of this method to neurophysiological data will be presented in the next section of this chapter.

3.0.2 Role of correlations in encoding of Information stimulus contrast in monkey visual cortex

Pairwise responses typically provide slightly more information, so that encoding is weakly synergistic. The simple comparison between pairwise and summed individual responses conflates several forms of correlation, however, making it impossible to judge the relative importance of synchronous spiking, basic tuning properties, and stimulus (in)dependent correlation. In this section we have applied an informa-

tion theoretic approach to this question, using the responses of pairs of neurons to drifting sinusoidal gratings of different orientations and contrasts, recorded in the primary visual cortex of anesthetized macaque monkeys. Our approach allows us to break down the information provided by pairs of neurons into a number of components. The results we present in this chapter are part of a work we have carried out in collaboration with Kohn and Smith (Montani et al., 2007).

We applied the information breakdown to investigate of how groups of neurons in primary visual cortex (V1) encode contrast and direction of motion of visual stimuli. To address this question, Kohn and Smith (Kohn and Smith, 2005) recorded, from area V1 of anesthetized macaques, responses of pairs of neurons to drifting sinusoidal gratings of different directions and contrasts. Using cross-correlation measures, they showed that an orientation sensitive component of the response correlation dominated at short time scales, and an orientation insensitive component was prevalent at longer time scales. In a subsequent analysis of the same data, we used the information breakdown to gain a more quantitative insights into the role of noise correlations in the encoding of contrast and orientation (Montani et al., 2007). Figure 4A summarizes the results, averaged over the whole population, of the breakdown of information about direction carried by pairs of neurons (Montani et al., 2007). For this analysis, the neural response of each pair was quantified as the spike count carried over a post-stimulus window of fixed length. Different
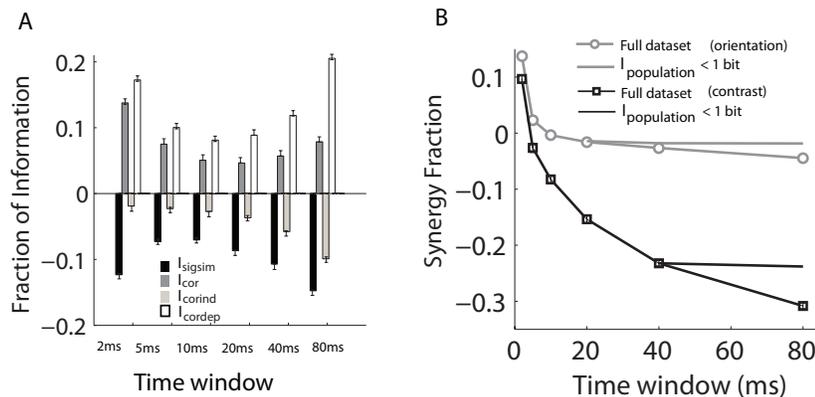

Fig. 4 The breakdown of information about stimulus direction carried by pairs of V1 neurons. Bar charts report the fraction of the information accounted for by the different components of the information breakdown plotted as function of the length of the post-stimulus time window used to compute the spikes (average $+/-$ s.e.m. over the entire data-sets). *B* The synergy fraction (defined as $1 - I_{sum}/I_{ensemble}$ and indicating the fraction of information beyond that expected if the cells are independent) is plotted against the time window used for counting spikes. The lines show the average ($+/-$ s.e.m.) over the entire dataset, and over only those pairs showing ensemble information lower than 1 bit (this latter curve excluding potential artefactual redundancy effects). The degree of redundancy in the coding of contrast quickly becomes substantial as the time window is increased. The results for contrast coding are indicated by squares and a black line; the results for direction coding (by the grey line and circles.
Reprinted from (Montani et al , *J Neurosci.* 2007)

window lengths (in the range 2-80 ms) were used. Figure 4A shows that the contribution of the information components is strongly dependent of the length of the response window: while the negative contribution of $I_{cor-ind}$ grows with the time window, the effects of the other components follow a 'U' or inverted "U" shape curve. For time windows lower than 10 ms, the preservation of temporally precise noise correlations (Kohn and Smith, 2005) resulted in correlational information which was a relatively large fraction of the total information $I(S; \mathbf{R})$ (Figure 4)A. At time windows longer than 10 ms the contribution from $I_{cor-dep}$ was significantly curtailed, and was effectively canceled by the signal similarity term, $I_{sig-sim}$, and also by $I_{cor-ind}$, which provided a greater negative contribution as the time window increased (Figure 4).

The picture over the entire population is one of a small amount of synergy: with a time window of 5 ms, the ensemble code does on average 2.4% better than the sum of single cell contributions (see Figure 4B). To compute the degree of synergy in the population for a range of time windows T, we calculated a synergy index
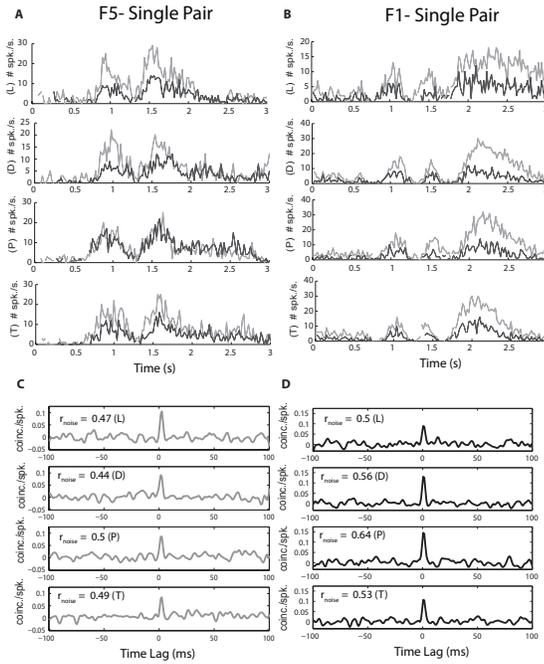
Fig. 5 A and B correspond to the PSTH and Cross-correlograms for the responses of a typical pair of cell in F5. C and D correspond to the PSTH and CCG of a typical pair of cell in F1. The Cross-correlation was estimated for the four stimuli conditions. The corresponding r_{noise} values are indicated in each panel. Cross-correlograms for the pair above show that fine-timescale synchronization is induced for stimuli that drive both cells relatively well.
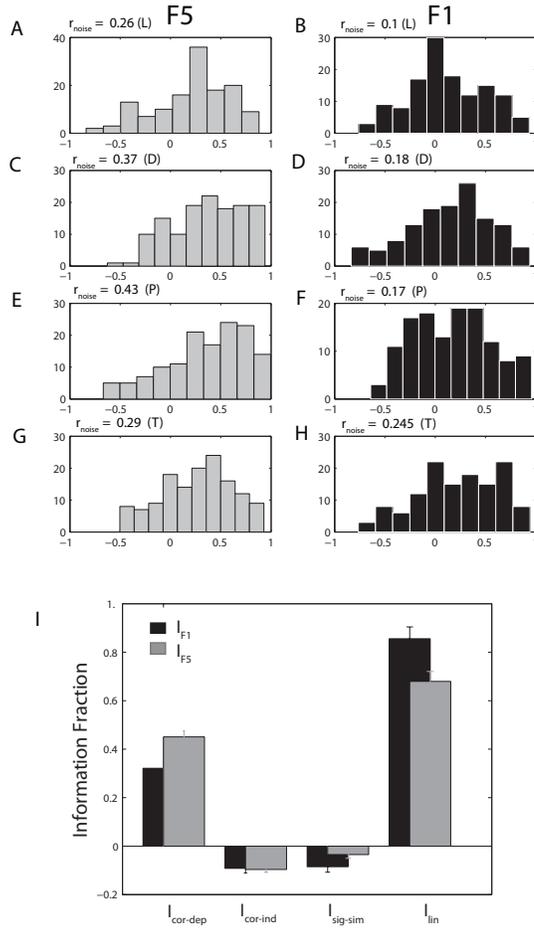
Fig. 6 A-H Relationship between the number of cells and r_{noise} (200 ms around 1s) for each of the four stimuli (twelve trials for each of them). We considered 137 pairs of neurons in F5 and 129 pairs of neurons in F1. The number next to each plot indicated by r_{noise} is the mean of the distribution. Full Light (L) population histograms of r_{noise} drove the pair most effectively in F1. I. Fraction of Information components across the entire population of neurons (137 pairs in F5, and 129 pairs in F1). We considered two bins of 200 ms around 1s. Error bars indicate standard deviation of the mean. The bar charts on the left side of the Figure capture the effects of the stimulus dependent synchronization component $I_{cor-dep}$, the bar charts that follow are the average level of correlation $I_{cor-ind}$, the signal similarity contribution, $I_{sig-sim}$, and the linear component I_{lin}. Notice that redundancy contributions due to the signal similarity term are higher for F1 than F5, and that the linear component I_{lin} is more informative for F1 than for F5.in other words, within the motor cortex information across pairs of cells adds linearly. This is not the case in F5 where information across pairs of cells adds super-linearly.

(which we call the synergy fraction) as $(I_{ensemble}\text{-}I_{sum})/I_{ensemble}$: values greater than zero indicates synergistic coding, values less than zero indicate redundancy. The synergistic effect of ensemble coding is more substantial at shorter time windows, where the fine temporal precision at which the spikes may synchronize has a significant effect – the maximum effect we observed was 13.7% at 2 ms (for technical reasons related to convergence of the numerical integral involved in the entropy computation, the smallest time window we were able to use), tailing off sharply at around 10 ms, where the synergy fraction is close to zero (Figure 4B). Thus, being very precise about spike timing leads to synergy rather than information independence (Schneidman et al., 2003). The short time scale over which synergy is present agrees well with the time scale of synchrony in the population: the mean full width at half maximum of the CCG peaks was 9 ms (Kohn and Smith, 2005). At longer time windows ($T \geq$ 20 ms), the information became comparable in size to the stimulus entropy ($\log_2$ 5 bits), and thus ceiling effects may reduce the raw information values somewhat. We corrected for this by removing pairs from the population that presented a higher information amount than 1 bits at a given time window, an arbitrary but conservative threshold. It is apparent that in the absence of ceiling effects, the trend for long time windows is for the synergy fraction to asymptote to a slightly negative value, indicating that the mutual information adds across the neurons as if they were roughly independent.

Notice that Figure 4B shows that the different stimuli responses convey redundant information about contrast, this is reasonable due to the fact that nearby neurons in V1 are tuned to similar stimulus features (Montani et al., 2007)..

We have found that for direction coding the information available by being precise about spike timing for pairs of neurons in V1 adds super-linearly. But as the timescale becomes more coarse, information about direction adds slightly sublinearly across pairs of cells in agreement with a previous information theoretic study of V1 cells (Reich et al., 2001). We have revealed the origin of these effects by our information component analysis, which shows a redundant (negative) contribution to the information due to the overlap in tuning and to the average level of correlation (i.e. stimulus independent correlation). However, these components are balanced on average by a contribution from stimulus-dependent synchrony.

To overcome the statistical inefficiency of high activity ratio distributed representations, which are the typical product of redundancy reduction code, one needs representations with minimum overlap. This is, representations with the minimum number of elements active in both inputs in pair of cells that need to be distinguished. However, our finding suggest that stimulus dependent correlations can help the neural code to overcome this problem. The fact that the synchronization depends on the stimulus direction is critically important for coding: it serves to reduce the redundancy caused by cells having similar tuning.

It is important to point out that this comes about because of a balance between the strong synergy provided by stimulus-dependent correlation and redundancy arising from the similarity in tuning of the neurons, and not because there are no signal and noise correlations. Although noise correlations are informative, the additional information they provides is frequently offset by the redundancy arising from the similar

tuning properties of the two cells. An interpretation of this result is that this cancelation this would allow cortical circuits to enjoy the stability provided by having similarly tuned neurons without suffering the penalty of redundancy as the associated information transmission deficit is compensated for by stimulus dependent synchrony (Montani et al., 2007).

The coding of contrast was far more redundant than that of direction at all time windows considered, because of the strong signal correlations in the coding of contrast (Montani et al., 2007). The results of this analysis warn strongly against making general statements about the role of correlations in neural coding – as demonstrated here, the effect of correlations can be quite sensitive to both the timescale and the nature of the stimulus parameter that is being studied.

3.0.3 Neural population coding of reach-to-grasp: the role of stimulus dependent correlations

Grasping is one the most evolved types of primate behavior, resulting from the transformation of a complex visuomotor process into specific motor commands required to reach-to-grasp an object. Higher order sensory and motor representations required in this process appear to emerge from the neuronal firing rate. It has yet to be determined whether pre-motor and motor neurons encode information only in the numbers of spikes each neuron emits or as well in the relative time of firing of the different neurons that might reflect synchronization. To address this question, we have applied an Information Theoretic approach to neuronal responses recorded in the premotor and motor cortex to four different Light stimulus conditions throughout the process of reach-to-grasp an object. We investigated if the synchronized firing of nearby neurons inside the premotor and motor cortex area can carry additional information about stimuli representation.

A quantitative answer to how correlation affects the neural coding, independent of how responses are decoded, can be provided by Information Theory (Panzeri et al., 1999; Pola et al., 2003; Montani et al., 2007) . The current study applies an Information Theoretic approach to investigate the neural code of reach-to-grasp. In doing so, we estimated the premotor and motor information conveyed by areas F5 and F1. We used neuronal responses to four different Light stimuli that have been recorded in the premotor and motor cortex of an unanaesthetized, partially restrained, macaque monkey (Montani, Oleynik, Caselli, Magri, Panzeri and Fadiga, 2009). To gain a quantitative understanding of how pre and motor cortical neurons might report the different stimulus, we investigated the role of correlation in stimulus encoding of the pre and motor cortex area.

When a stimulus is shown repeatedly, trial-to-trial fluctuations in response strength are correlated between neighboring cortical neurons. This correlation is typically characterized by the spike count correlation r_{noise}. The timing of action potentials of nearby neurons is also often correlated or synchronized (Kohn and Smith, 2005; Montani et al., 2007). Thus, it is important to focus our attention also on how pairs of cells with common inputs and similar receptive fields might be affected by spike

synchrony. It is unclear, however, how synchrony between single neurons within F5 and F1 are affected by basic light stimulus manipulation: Full Light (L), Full Dark (D), Pre-touch (P) flash light, and Touch flash light(T). Characterizing correlation and its stimulus dependence is important for understanding the computations that can be performed by a neuronal population.

Figure 5 A, B show the PSTH for two typical pairs of cells in F5 and F1. Figure 5C and D show the cross-correlograms for the same pairs of cells. The correlation is characterized using a (shift predictor corrected) spike train cross-correlogram (CCG; (Perkel et al., 1967)). We presented four stimuli that drove each cell through the firing rates. The result is a substantial modulation in the height of the central peak of the cross-correlogram of the neurons' spike trains: at a particular orientation that drives both neurons moderately well, a fraction of the spikes fired by each neuron tend to be synchronized with millisecond temporal precision. This result can be verified for both F5's and F1's pairs of neurons as showed in Figure 5C,D. This stimulus dependence of synchrony arises despite correcting for the basic rate dependence of the CCG.

As we have mentioned previously neurophysiologic experiments can only convey a finite number of trials, and therefore the true stimulus-response probabilities cannot be estimated exactly. The estimated probabilities fluctuate around their true values and due to small number of trial it was crucial to use an effective sampling procedure. For the purpose of the information calculations, we use three equi-populated response bins with fixed time window lengths T=100ms. This is to say, in order to facilitate the sampling of its probability, we discretized the response space by binning each time window of T=100ms into equipopulated bins. To correct sampling we used a quadratic extrapolation procedure (QE, Strong et al., 1998) to estimate and subtract out the bias of each information quantity. For the current analysis, we found that the quadratic extrapolation QE (Strong et al., 1998) was the most stable. Panzeri-Treves (Panzeri 1996) method to remove sample size dependent bias from the entropy estimations does not perform well for such number of trails, if the binning is not constant across the ensemble. The pair-wise information $I(S; r1r2)$ conveyed by the joint observation of two cells was also estimated using the "shuffling procedure" described by (Montemurro et al., n.d.; Panzeri et al., 2007), which greatly reduces the bias of multidimensional information estimates. We chose $R = 3$ because it was the biggest number that consistently led to robust unbiased results under the sampling conditions of our experiment. The performance of the "shuffling procedure" procedure on realistically simulated neural spike trains has been reported in detail previously by others authors (Montemurro et al., n.d.; Panzeri et al., 2007).

Figure 6 shows the Information component breakdown I_{sh}, $I_{cordep-sh}$, and I_{lin} of premotor and motor cortex neuronal responses within a time window of 200 ms around the precise moment in which grasping is taking place(denoted by now on as '1s'). Correlational effects are captured by the stimulus dependent synchronization component, $I_{cor-dep}$, and by the average level of correlation $I_{cor-ind}$. Notice that $I_{cor-dep}$ is strongly related to the extent of synergistic coding within pre-motor and motor areas. The average level of correlation $I_{cor-ind}$ takes higher negative values for F1 than for F5. Surprisingly, the linear component I_{lin}, which represents the

information that would be obtained if each neuron were to convey independent information, is more informative for F1 than for F5. The signal similarity term $I_{sig-sim}$ reflects the redundant contribution due to the overlap in tuning curves. In our current analysis, I_{sigsim} takes higher negative values for F1 than for F5, which is in agreement with the averaged signal correlation values r_{signal}, estimated through the Person correlation. Overall, our findings show that the pair-wise coding of reach-to-grasp is more informative for F1 than for F5. The picture over the entire population of pairs in F5 is one of a very important amount of synergy: with a time window of 200 ms 'around 1s', the ensemble population $I_{population}$ code outperforms the mean of single cell Information values I_{lin} by 32 % on average. The linear term in the case of F5, I_{lin} , accounts only for 68 % of the total ensemble information, and stimulus component correlation $I_{cor-dep}$ corresponds to 45 % of the total information. In contrast, notice that in F1 the amount of synergy is less than half of the value obtained for F5 (the population ensemble perform on average 14,45% better than the sum of single cell contributions, see Figure 6I). Thus, information across pairs of cells in F1 is roughly independent, whereas information across pair of cells in the pre-motor cortex area F5 adds super-linearly. It is important to point out that due to the small number of trial (12 trails) it was crucial to use an effective sampling procedure. For the current analysis, we found that the quadratic extrapolation QE (Strong et. al 1998) was the most stable. The method of Panzeri-Treves (Panzeri and Treves, 1996) methods to remove sample size dependent bias from the entropy estimations does not perform well for such number of trails, if the binning do not remain constant across the ensemble.

In our study, the stimulus-dependent correlation component $I_{cor-dep}$ was sufficiently large to outweigh redundant effects due to the average level of correlation ($I_{cor-ind}$) leading to an overall synergistic effect of correlations. Our results suggest that there is a significant amount of synchronous spike between pair of cells in both premotor and motor cortex area. In the case of F5, the stimulus dependent correlation component, $I_{cor-dep}$, is about 15 % higher than in F1. Moreover, $I_{cor-dep}$ is about 45% of the total (shuffled) information (I_{sh}) in F5, whereas in F1 the stimulus dependent correlation component $I_{cor-dep}$ is smaller. $I_{cor-dep}$ is about 32 % of the total shuffled information (I_{sh}) in F1. This is a significant amount of synchrony in both areas effectively providing additional information about the stimuli beyond the information provided by the independent firing.

The analysis performed over pair-wise responses suggests that correlations in the trial-to-trial response variability are more likely to increase than decrease information content. Information across pairs of cells in F1 is roughly independent, whereas information across pair of cells in the premotor cortex area F5 adds super-linearly. Thus, pair-wise synchronization could be seen as a requirement to perform the synergistic movement needed to achieve the process of reach-to-grasp. The brain could take advantage of both the accuracy provided by independency in F1 and the synergy allowed by the super-linear informational population code in F5. This suggests that pair-wise interactions between neurons help to bring about internal representation of visuomotor information into specific motor command throughout the process of reach-to-grasp.

4 Conclusions

Other studies have applied some or all of the information component analysis discussed above to to simultaneously recorded pairs of neurons from the visual cortex (Golledge et al., 2003; Montani et al., 2007; Rolls et al., 2003) or retina (Nirenberg et al., 2001). A results which is highly consistent across all such experiments is that $I_{cor-dep}$ is relatively small, in most cases about the 10 % of the total mutual information.

The amount of $I_{cor-dep}$ is expected to be larger in the premotor and motor cortex areas (Stark et al., 2008), and we found substantial stimulus dependent correlation between pair of neurons in F1 and F5. These results are consistent with the idea that the higher level of attention to stimuli boosts neuronal responses and enhances the level of synchronization (Kim et al., 2007). Thus, pair-wise synchronization can be seen in this example as a requirement to perform the synergistic movement needed to achieve the process of grasping.

It is important to point out that even if the impact of correlations is "relatively small" at the level of neuron pairs they could have a much stronger effect at the level of larger populations. More specifically, in a recent study we analysed 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. We showed that high-order interactions could 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 (Montani, Ince, R., Arabzadeh, Diamond and S., 2009). Thus, an open challenge in Theoretical Neuroscience is to extend the techniques applied in this chapter in order to account for signal and noise spike correlations of higher order than two.

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