

# Redundancy and Synergy of Neuronal Ensembles in Motor Cortex

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We examined the ability of neuronal ensembles from rat motor cortex to predict behavioral performance during a reaction time task. We found that neurons that were the best individual predictors of task performance were not necessarily the neurons that contributed the most predictive information to an ensemble of neurons. To understand this result, we applied a framework for quantifying statistical relationships between neurons (Schneidman et al., 2003) to all possible combinations of neurons within our ensembles. We found that almost all neurons (96%) contributed redundant predictive information to the ensembles. This redundancy resulted in the maintenance of predictive information despite the removal of many neurons from each ensemble. Moreover, the balance of synergistic and redundant interactions depended on the number of neurons in the ensemble. Small ensembles could exhibit synergistic interactions (e.g., 23 ± 9% of ensembles with two neurons were synergistic). In contrast, larger ensembles exhibited mostly redundant interactions (e.g., 99 ± 0.1% of ensembles with eight neurons were redundant). We discuss these results with regard to constraints on interpreting neuronal ensemble data and with respect to motor cortex involvement in reaction time performance.

**Key words:** motor cortex; population coding; neuronal ensembles; reaction time; synergy; redundancy

## Introduction

How do ensembles of cortical neurons work together to encode information? Pioneering studies of motor cortex by Georgopoulos et al. (1982, 1988) have suggested that “population vectors,” constructed from weighted averages of the responses of single neurons, can accurately predict behavioral variables, such as movement direction. This approach has been used to study population coding in a number of cortical systems (Gochin et al., 1994; Britten et al., 1996; Priebe and Lisberger, 2004; Romo et al., 2004). These studies have led to the view that cortical neurons act as independent processors of information (Gochin et al., 1994; Rolls et al., 1997, 2004; Reich et al., 2001; Purushothaman and Bradley, 2005). Although correlations between neurons may be important factors for neural coding (Zohary et al., 1994; Vaadia et al., 1995; Dan et al., 1998; Abbott and Dayan, 1999; Bair et al., 2001; Nirenberg and Latham, 2003; Averbeck and Lee, 2004; Johnson, 2004), few studies have demonstrated that considering neuronal interactions increases predictive information over that

contained in individual neurons (Riehle et al., 1997; Hatsopoulos et al., 1998; Gat and Tishby, 1998; Maynard et al., 1999; Averbeck et al., 2003; Samonds et al., 2004).

Gawne and Richmond (1993) and, more recently, Schneidman et al. (2003) have proposed a theoretical framework for interpreting neuronal ensemble activity in which information encoded by an ensemble of neurons is compared with the sum of information encoded by the component neurons. In this framework, an independent coding scheme suggests that predictive information encoded by an ensemble of neurons should approximately equal the sum of its individual parts. However, if ensemble interactions exist between recorded neurons, interactions can be either synergistic (i.e., predictive information encoded by the ensemble of neurons is greater than the sum of the information of the individual neurons) or redundant (i.e., the predictive information encoded by the ensemble is less than the sum of information of individual neurons). With redundancy, a hallmark of distributed processing, the removal of individual neurons from an ensemble does not affect overall system performance. Redundant systems are thus resistant to error and can have improved signal-to-noise (Barlow, 2001).

In the present study, we investigated the relationship between ensembles of simultaneously recorded cortical neurons and their component neurons by using statistical classifiers to estimate predictive information at the individual-neuron and ensemble levels. We found that relationships between the activity of multiple neurons (that is, joint activity of neuronal ensembles) are important factors for the performance of statistical classifiers in predicting behavioral outcomes. We report three results: (1) the predictive information of a single neuron is not related to its informational contribution to a neuronal ensemble; (2) this ef-

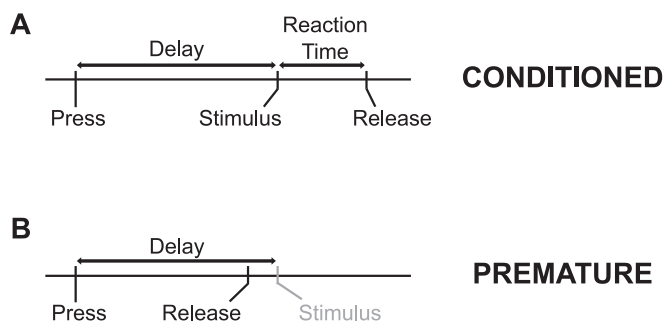
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**Figure 1.** The simple reaction time task, in which rats were trained to initiate a trial by pressing a lever, which they held for a variable delay lasting 400–800 ms. The rats received a vibrotactile or an auditory stimulus. **A**, On conditioned release trials, rats performed the task appropriately and released the lever within 1 s of the conditioning stimulus to receive a water reward. **B**, On premature release trials, rats released the lever prematurely before they received the vibrotactile or auditory stimulus. If the response was premature, there was a 2 s timeout. Note that the stimulus (represented in gray) did not occur on premature trials.

fect is attributable to high levels of redundancy; and (3) the extent of redundant or synergistic interactions depends on the size of the neuronal ensemble. Ensembles of more than a few neurons were almost entirely redundant. Smaller ensembles of neurons, especially pairs or triplets, could be either redundant or synergistic.

## Materials and Methods

### Behavioral and electrophysiological methods

Data were collected from the motor cortex of awake rats performing a simple reaction time task (Laubach et al., 2000). Adult, male rats (Long-Evans) were trained to perform a simple reaction time task (Fig. 1). In this task, the rats pressed a lever to initiate a trial and maintained the lever press over a variable delay period of 400–800 ms. At the end of the delay, a trigger stimulus was presented (tone or vibration of the lever), and the rats released the lever within 1 s of stimulus onset to obtain a reward (~0.02 ml of water). “Conditioned” responses in the task occurred when the rats successfully maintained the lever press for the full delay period and released the lever within 1 s of the trigger stimulus. “Premature” responses occurred when the lever was released before the trigger stimulus. “Late” responses occurred when the lever was released >1 s after the trigger stimulus and were infrequent after initial training sessions (<10% of trials). In the present study, neuronal ensemble activity was compared for trials with conditioned and premature responses. Data analysis was performed for two sessions from each of three rats. These data were collected after several weeks of training, i.e., some time after the data described in the study by Laubach et al. (2000).

Procedures for chronically implanting arrays of microwire electrodes (NB Labs, Denison, TX) are described in detail previously (Nicolelis, 1998). Two chronic microwire arrays (50  $\mu$ m stainless steel wire, Teflon insulation to a blunt tip, arranged in  $2 \times 8$  matrices with individual wires spaced by 250  $\mu$ m) were stereotaxically implanted in rat motor cortex (caudal array:  $-0.5$ – $1.0$  mm anteroposterior,  $\pm 2.5$ – $3.5$  mm mediolateral,  $-1.5$  mm dorsoventral at  $-20^\circ$  anterior to the frontal plane; rostral array:  $+2.0$ – $3.5$  mm,  $\pm 2.0$ – $3.0$  mm,  $-1.5$  mm at  $+20^\circ$  posterior to the frontal plane; coordinates from bregma) under aseptic conditions. The locations of microwires were reconstructed from 50- $\mu$ m-thick, thionin-stained, frontal sections after the completion of all experiments. All rats were treated in accordance with National Institutes of Health guidelines.

Neuronal ensemble recordings were made using a many-neuron acquisition program (MNAP; Plexon, Dallas, TX). Single neuronal units were identified off-line by the following criteria: consistent waveform shapes, an average waveform amplitude at least three times larger than background activity, and a consistent refractory period of at least 2 ms in interspike interval histograms. Only units whose activity was modulated around the time of lever release were analyzed, as assessed visually by using cumulative density plots (Stranger; Biographics, Winston-Salem, NC).

The animals’ behavior was recorded on videotape and examined to ensure that it was consistent for all trials included in a given analysis. Additional control data were collected in one animal in which neuronal ensemble activity was recorded together with electromyographical (EMG) data (agonist: triceps brachii, which extends the forelimb; antagonist: trapezius, which rotates and pulls the shoulder blade toward the spinal column). Additionally, an electrolytic tile sensor (Advanced Orientation Systems, Linden, NJ) was mounted on the response lever and recorded the angle of the lever. Signals from the EMG electrodes and the positional sensor were amplified and filtered at 20–500 Hz (SA Instrumentation, Encinitas, CA) and sampled at 1 kHz. As described by Laubach et al. (2000), there were no significant differences between the evoked EMG or lever-position data that accompanied lever releases on trials with conditioned versus premature responses.

### Data analysis

A statistical pattern recognition approach was used to quantify the predictive relationship between neuronal activity and the behavioral outcome of each trial (i.e., conditioned vs premature response). This approach involves three basic steps that are described below: (1) preprocessing, (2) dimension reduction, and (3) prediction of behavior using statistical classifiers.

**Preprocessing.** Neural activity was collected from 400 ms before to 100 ms after lever release. For each neuron, average spiking responses for conditioned and premature trials were computed using a bin size of 1 ms. Single-trial perievent time histograms of neural activity were then convolved over 5 ms epochs using low-pass filtering (Richmond and Optican, 1987) and decimation (for additional details, see Laubach, 2004). This low-pass filtering was performed on the raw perievent histograms before the wavelet packet analysis below.

**Dimension reduction.** A wavelet-based method, discriminant pursuit (Buckheit and Donoho, 1995; Laubach, 2004), was used to reduce the dimensionality of the neuronal data before analysis with statistical classifiers. This was performed in four steps, as follows. First, a difference vector was computed for each neuron by subtracting the mean response on different types of trials (i.e., conditioned vs premature response). Second, the difference vector was decomposed with the wavelet packet transform using the Daubechies four-tap wavelet. The result of the wavelet packet transform is several components, analogous to components in principal component analysis. Each wavelet component represents variance in the original data and corresponds to a “feature” in the firing pattern of a single neuron, such as an increase in firing rate preceding movement on conditioned trials. Third, wavelet components were ranked by the between-groups variance that they accounted for in the original spike trains. Finally, a reduced set of components was then chosen for subsequent analysis by using only those features from a given neuron that accounted for more variance than features extracted from random data; that is, the amplitudes of features extracted from neural data were compared with those extracted from 1000 “random” data sets, in which the outcome of each trial was assigned pseudorandomly. This approach is an alternative to using an arbitrary criterion for determining the number of features (cf. Laubach, 2004). In the present study, neurons with task-related features had an average of  $5.5 \pm 2.5$  features. Interactions between neurons were not examined at this stage of processing. Instead, neuronal interactions were evaluated using statistical classifiers described below.

**Statistical classification.** Features obtained with the wavelet packet analysis were subsequently used as input for a variety of statistical classifiers. Exploratory analysis of statistical classifiers was conducted in R (Venables and Ripley, 2002; Venables et al., 2004) and in WEKA (<http://www.cs.waikato.ac.nz/~ml/weka/>; WEKA is a data mining tool that enables rapid processing of data and visualization of results with a multitude of classifiers). We selected three classifiers for additional analysis: learning vector quantization (LVQ) (Kohonen, 2000) (we chose LVQ because previous studies have used it; see below), penalized discriminant analysis (PDA) (Hastie et al., 1995) (we chose PDA because it is a linear method), and support vector machines (SVMs) (Hastie et al., 2001; Hsu et al., 2003) (we chose SVMs because they performed well). LVQ was implemented using the “class” library for R. An algorithm for SVMs

(libSVM) with a sigmoid transfer function was implemented using the “e1071” library for R, and PDA, which involves the use of ridge regression to define discriminant functions that are subsequently analyzed with a Gaussian mixture model, was implemented using the “mda” library for R (of special note, the algorithms for these implementations in R used original source code developed by the authors of each algorithm.) No effort was made to optimize parameters of any statistical classifiers in this study. All results were confirmed with multiple classifiers; however, for the purposes of comparison with previously published papers (Nicolelis et al., 1998a; Ghazanfar et al., 2000; Laubach et al., 2000; Furukawa and Middlebrooks, 2001; Middlebrooks and Bierer, 2002), the results in this manuscript were described using LVQ, except when explicitly reported.

The statistical classifiers were trained on subsets of trials (i.e., training data), and predictions were made for trials not included in the training data (i.e., testing data). To generate stable estimates of predictive information, 10-fold cross validation was used; that is, each trial was a member of one testing data set and a member of nine training data sets. The result of each statistical classifier is a “classification matrix” (also called a confusion matrix); that is, a table of correct and error predictions by the classifier for each class on the testing data.

For every value of information and accuracy reported, error bars were estimated by performing 10 10-fold cross validations (100 classifications). Chance levels of classification and confidence intervals were estimated by permutation tests (Good, 2000) in which the behavioral labels for all trials were randomly permuted, and classification analysis was repeated 1000 times with a unique random seed for each iteration.

All analysis described in this manuscript was performed using scripts written for R, WEKA, and Matlab (MathWorks, Natick, MA). These analyses were run over a cluster of 16 Linux workstations via batch scripts in the Bash shell. All analysis and clustering scripts used in this study are available on request from the corresponding author.

**Limitations of statistical classifiers.** In this study, statistical classifiers were used to predict a behavioral condition (i.e., conditioned vs premature response) from neural data as represented by features from multiple neurons. Information contained in the neural data were estimated by applying information theory to confusion matrices for each classifier and each data set (see below). It is important to point out that this approach cannot estimate the true mutual information contained in the neuronal data because the informational estimates depend on the specific classifier used for prediction (for review, see Ripley, 1996; Duda et al., 2001; Hastie et al., 2001). Consequently, several different statistical classifiers were used when estimating neural information. However, it is always possible that another statistical classifier exists that will perform better on our data. Even if such a classifier exists, there is no way to verify that rules used by a statistical classifier have any relationship to the true mutual information or rules used by the animal. For these reasons, and according to the data processing inequality (Cover and Thomas, 1991; Schneidman et al., 2003), we and others (Averbeck et al., 2003; Foffani et al., 2004) can only estimate a lower bound of mutual information between neural data and behavioral outcomes. Nevertheless, we believe that the statistical pattern recognition approach is a practical solution to the problem of interpreting high-dimensional neuronal ensemble data. This approach has been used for a variety of real-world datasets (Ripley, 1996; Witten and Frank, 2000; Hastie et al., 2001) and is able to quantify relationships between neurons and animal behavior on a trial-by-trial basis (compared with information theoretic methods, which are average measures).

**Assessment of classifier performance.** Statistical classifier performance can be assessed in several ways. One index of statistical classifier performance is “error rate,” or the number of trials classified incorrectly divided by the total trials. For clarity, “accuracy” ( $1 - \text{error rate}$ ) is reported in this manuscript. Note that the chance accuracy is not 50%; rather, it is the percentage of trials in the larger class.

One method of assessing statistical classifier performance that allows us to compare our results with other neuroscientific studies is to calculate mutual information (Gawne and Richmond, 1993; Rolls et al., 1997; Ghazanfar et al., 2000; Laubach et al., 2000; Reich et al., 2001; Schneidman et al., 2003). We calculate the mutual information from the classification matrix according to the following equation (Cover and Thomas, 1991):

**Table 1. Illustration of combinations for three neuron ensemble**

Ensembles with neuron 3		Ensembles without neuron 3
3 2 1	→	2 1
3 2	→	2
3 1	→	1
3	→	N/A

$$I(S; R) = \sum_{s \in S} \sum_{r \in R} p(s, r) \log_2 \left[ \frac{p(s, r)}{p(s)p(r)} \right] \quad (1)$$

where  $S$  is the actual outcome, and  $R$  is the predicted outcome. In general, measures of statistical classifier performance are highly correlated. Accuracy and mutual information for individual neurons were correlated at  $R = 0.94 \pm 0.04$  ( $t \gg 10$ ;  $p \ll 0.001$ ).

**Bias and variance.** There are two sources of error in estimates of mutual information from the statistical pattern recognition approach: “bias” and “variance” (Ripley, 1996; Hastie et al., 2001). Bias refers to error between estimates of predictive information and true information. For statistical classifiers, there are three sources of bias. First, a statistical classifier might have a “language bias” based on its representational ability; that is, some algorithms may be better able to capture certain types of data as a function of the way they internally represent that data. Second, statistical classifiers might suffer from a “search bias” in the heuristic rules that they use to fit the data. If the rules are inappropriate, inaccurate conclusions may be reached. Finally, statistical classifiers can suffer from an “overfitting bias,” or tendency to find patterns that do not exist in the data. For an additional discussion of these topics, see Witten and Frank (2000) or Hastie et al. (2001). The first two sources of bias were addressed by using multiple statistical classifiers with distinct internal representations and decision rules. It is always possible that there exists another classifier that has an internal representation that better matches our data or that has more appropriate decision rules. The last source of bias, attributable to overfitting, was addressed directly in two ways. First, for every dataset and every number of neurons, the statistical pattern recognition approach was applied to data in which the behavioral labels for all trials were randomly permuted (see Results). Second, statistical classifiers were applied to benchmark data with a known Bayesian error rate (the “waveform” benchmark data, available in the “mlbench” library for R; 86% error rate), and it was found that these classifiers did not greatly overfit or underfit the benchmark data (generally within  $\pm 1\%$ ) (see Table 3, row 1). These tests lent confidence to our interpretations of the results of this study. The second source of error in classification was variance, i.e., errors in classification attributable to the sample chosen from which mutual information was predicted. Variance in our data were accounted for by repeating classifications several times.

#### Synergy and redundancy

To assess the contributions of each neuron to ensemble information, features for each neuron were removed from each ensemble, and the predictive information from the remaining neurons was estimated (i.e., “neuron dropping”) (Nicolelis et al., 1998b). The information contributed to the ensemble by a given neuron ( $I_{\text{Contrib}}$ ) was defined as the difference between the predictive information of the full ensemble ( $I_{\text{Ensemble with neuron}}$ ) and the predictive information of a subensemble without a given neuron ( $I_{\text{Ensemble without neuron}}$ ):

$$I_{\text{Contrib}} = I_{\text{Ensemble (with neuron)}} - I_{\text{Ensemble (without neuron)}} \quad (2)$$

Because a given neuron can participate in several subensembles of the original ensemble [for instance, for a three-neuron ensemble, neuron 3 participates in subensembles (2, 3), (1, 3), and (1, 2, 3)],  $I_{\text{Contrib}}$  was calculated for each of these subensembles that a given neuron participated in (for an illustration of the computation, see Table 1) by applying Equation 2 to all possible subensembles including a given neuron. Although computationally intensive (e.g., a data set with 17 neurons has 131,071 subensembles, requiring 182 h of CPU time to analyze all combinations of neurons using a single AMD 1800 XP processor; this same

data set could be analyzed in 13 h using a cluster with workstations with 16 processors), this analysis provided a robust estimate of  $I_{\text{Contrib}}$ . Within each ensemble,  $I_{\text{Contrib}}$  was compared only with ensembles of similar size (i.e., an average  $I_{\text{Contrib}}$  for 2, 3, 4...  $n$  neuron ensembles was calculated separately).

To measure how a particular neuron interacts with the rest of the ensemble, we defined a notion of information contributed by single neurons to the ensemble,  $P_{\text{Neuron}}$ . This value was calculated from the contribution of a neuron to ensemble predictive information subtracted from the individual predictive information of that neuron:

$$P_{\text{Neuron}} = I_{\text{Contrib}} - I_{\text{Neuron}} \quad (3)$$

In Equation 3,  $I_{\text{Contrib}}$  is the contribution of a particular neuron to an ensemble as measured by the predictive information lost after removing that neuron from an ensemble as calculated by Equation 2, and  $I_{\text{Neuron}}$  is the predictive information (in bits) encoded by that neuron.

This equation answers the following question: how does removing a neuron from an ensemble change ensemble predictive information? There are three possible results for removing a neuron from an ensemble that define the type of net contribution made by a neuron to information at the ensemble level. If  $P_{\text{Neuron}}$  is zero (i.e., if  $I_{\text{Contrib}} \approx I_{\text{Neuron}}$ ), then the information lost by removing a neuron is equal to the individual information encoded by that neuron. Such a neuron contributes “independent” information to the ensemble. Second, if  $P_{\text{Neuron}}$  is negative (if  $I_{\text{Contrib}} < I_{\text{Neuron}}$ ), the information lost by removing a neuron is less than the individual information encoded by that neuron. Such a neuron contributes “redundant” information to the ensemble. Third, if  $P_{\text{Neuron}}$  is positive (if  $I_{\text{Contrib}} > I_{\text{Neuron}}$ ), the information lost by removing a neuron is greater than the individual information encoded by that neuron. Such a neuron contributes “synergistic” information to the ensemble.

Interactions at the ensemble level were defined as  $P_{\text{Ensemble}}$  based on the ensemble information and the sum of the individual information of its component neurons:

$$P_{\text{Ensemble}} = I_{\text{Ensemble}} - \sum_1^N I_{\text{Neuron}} \quad (4)$$

where  $I_{\text{Ensemble}}$  is the predictive information of the ensemble, and  $I_{\text{Neuron}}$ , as above, is the predictive information of individual neurons in the ensemble.

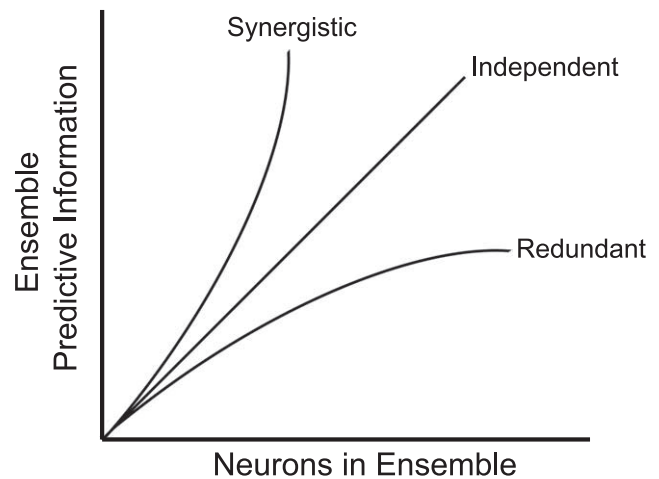
This equation answers the following question: how do neurons work together to encode predictive information? As above, there are three possible coding schemes. First, if  $P_{\text{Ensemble}}$  is zero, ensemble predictive information is the same as the sum of predictive information from neurons in the ensemble. As a whole, this ensemble is neither redundant nor synergistic. Second, if  $P_{\text{Ensemble}}$  is negative, ensemble predictive information is the less than the sum of predictive information from neurons in the ensemble. As a whole, this ensemble is redundant. Third, if  $P_{\text{Ensemble}}$  is positive, ensemble predictive information is greater than the sum of predictive information from neurons in the ensemble. As a whole, this ensemble is synergistic (Fig. 2).

In this manuscript, the quantities  $I_{\text{Contrib}}$  and  $P_{\text{Ensemble}}$  were calculated across all possible subensembles for a given data set (Table 2). Because these values were predictive information from classification, their units were expressed in bits. Also, note that Equation 2 assumes that the estimated informational values of each neuron in a given ensemble did not depend on each other. Although our estimates of predictive information were generated from statistical classifiers instead of from direct information theoretic measures, our results are analogous to those obtained in previous studies (Gawne and Richmond, 1993; Maynard et al., 1999; Averbeck et al., 2003; Schneidman et al., 2003; Samonds et al., 2004).

## Results

### Neuronal and ensemble predictive information

We analyzed ensemble neuronal data from three awake, behaving rats performing a simple reaction time task (Laubach et al., 2000). Recording sessions (two from each rat) yielded an average of



**Figure 2.** Because neurons are added to an independent ensemble, predictive information increases proportionally to the number of neurons in the ensemble. If the ensemble is redundant, predictive information increases slower than the number of neurons added to the ensemble. If the ensemble is synergistic, predictive information increases faster than the number of neurons added to the ensemble.

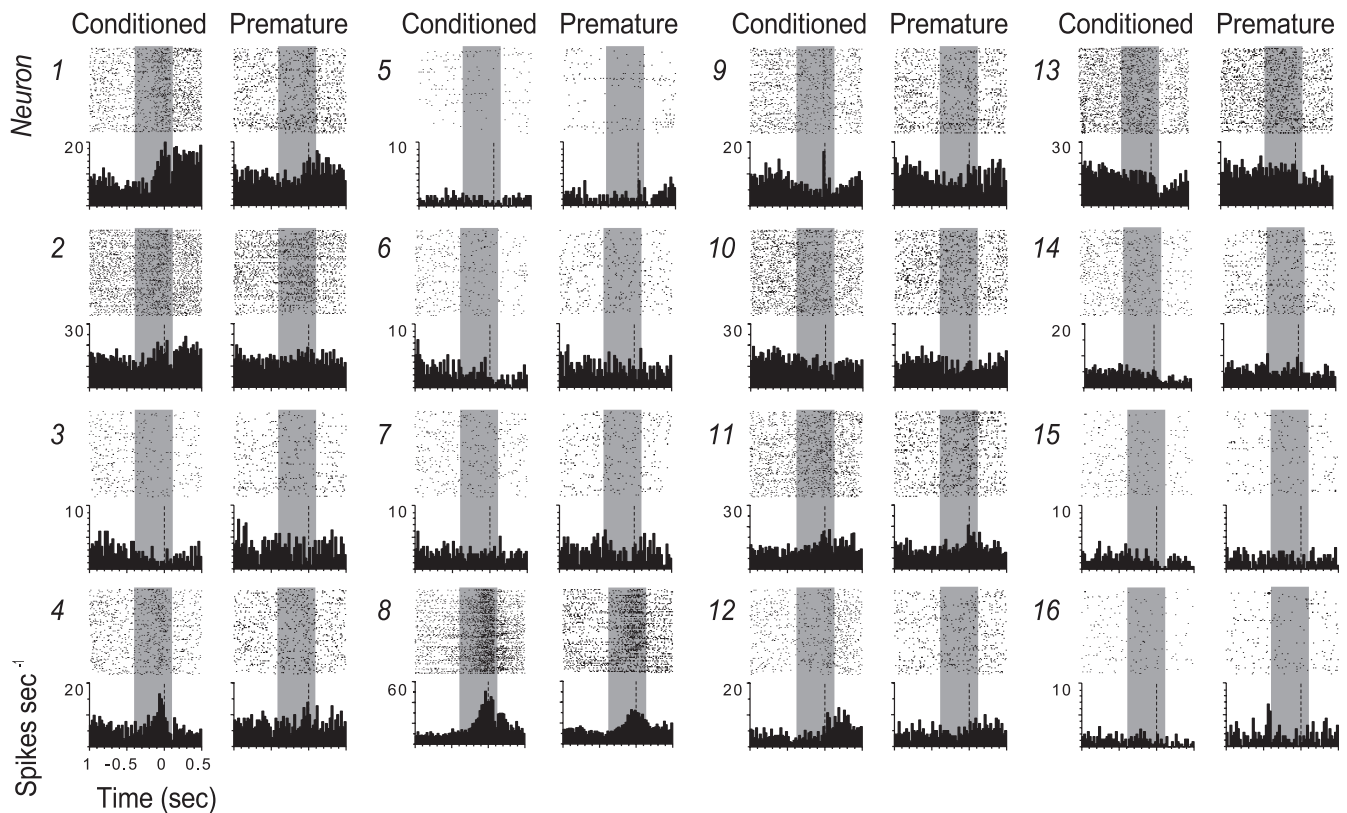
**Table 2. Ensemble combinations**

Dataset	Neurons	Features	Combinations
A1	16	84	65,535
A2	17	102	131,071
B1	8	57	255
B2	11	51	2047
C1	13	50	8191
C2	13	76	8191

$23.5 \pm 5.2$  (mean  $\pm$  SD) neurons (range of 17–27 neurons, 140 neurons total, 32 electrodes per animal performing  $195 \pm 33$  trials per session). Of recorded neurons, 55.5% (78 of 140 recorded neurons, or an average of 13 neurons per session) had task-related features, i.e., had more features than would be expected from random data (see Materials and Methods) (Fig. 3).

Analysis using statistical pattern recognition (preprocessing/discriminant pursuit/LVQ, unless otherwise stated) revealed that the single neurons could be used to discriminate between conditioned and premature trials with an average accuracy of  $68 \pm 3\%$  (accuracy for individual neurons with randomly permuted behavioral labels was  $64 \pm 8\%$ ). Using LVQ, the average single neuron encoded  $0.034 \pm 0.03$  bits of predictive information ( $I_{\text{Neuron}}$ ) of a possible  $0.90 \pm 0.02$  bits of predictive information [note that the possible information is  $< 1$  because, in every dataset, there are more conditioned vs premature trials (Table 3)] or  $4 \pm 3\%$  of the possible  $0.90 \pm 0.02$  bits of predictive information (Fig. 4). Using SVM for classification, the average single neuron encoded  $0.025 \pm 0.03$  bits of predictive information, and, using PDA for classification, the average single neuron encoded  $0.046 \pm 0.04$  bits of predictive information.

To determine chance levels of significant predictive information, we calculated predictive information from neural datasets with randomly permuted behavioral labels (i.e., random data). Across datasets, the 95% confidence interval of predictive information of random data fell at  $0.016 \pm 0.003$  bits (average predictive information was  $0.004 \pm 0.005$  bits). We interpreted values of predictive information above this value as significant. We found that 58% (45 of 78) of neurons with task-related features had predictive information above the 95% confidence intervals of



**Figure 3.** Perievent rasters and time histograms for an ensemble of 16 neurons with task-related features recorded from the motor cortex of one animal (dataset A1) while performing a simple reaction time task. A time interval from 400 ms before the lever release to 100 ms after (period shown in gray, release indicated by dashed vertical line) was used for the analyses reported in this study. Neurons 1–13 are from the caudal motor cortex, whereas neurons 14–16 are from the rostral motor cortex.

**Table 3. Statistical classifier performance across datasets**

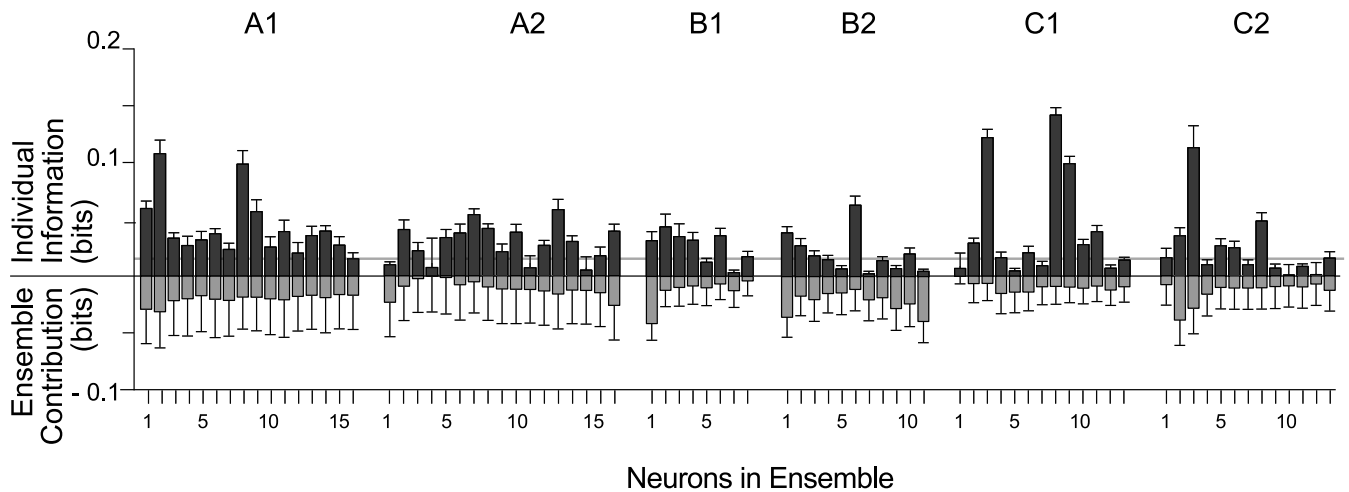
Dataset	Trials	Behavioral performance		Individual neuron	Chance	PDA	Chance	SVM	Chance	LVQ	$P_{\text{Ensemble}}$	
Benchmark	3000	Acc				$86 \pm 1\%$		$86 \pm 1\%$		$87 \pm 3\%$		%
		Info				$0.87 \pm 0.00$		$0.85 \pm 0.00$		$0.89 \pm 0.00$		Bits
A1	173	58%	Acc	$64 \pm 3\%$	<i>54</i>	$86 \pm 1\%$	<i>56</i>	$89 \pm 2\%$	<i>56</i>	$79 \pm 2\%$		%
			Info	$0.05 \pm 0.03$	<i>0.01</i>	$0.39 \pm 0.03$	<i>0.01</i>	$0.50 \pm 0.05$	<i>0.01</i>	$0.23 \pm 0.04$	$-0.43$	Bits
A2	163	63%	Acc	$65 \pm 2\%$	<i>52</i>	$77 \pm 1\%$	<i>60</i>	$91 \pm 1\%$	<i>57</i>	$79 \pm 1\%$		%
			Info	$0.03 \pm 0.02$	<i>0.01</i>	$0.19 \pm 0.02$	<i>0.01</i>	$0.52 \pm 0.04$	<i>0.01</i>	$0.22 \pm 0.02$	$-0.31$	Bits
B1	171	76%	Acc	$77 \pm 1\%$	<i>64</i>	$81 \pm 2\%$	<i>75</i>	$84 \pm 1\%$	<i>75</i>	$79 \pm 1\%$		%
			Info	$0.03 \pm 0.01$	<i>0.00</i>	$0.13 \pm 0.03$	<i>0.00</i>	$0.18 \pm 0.03$	<i>0.01</i>	$0.07 \pm 0.02$	$-0.14$	Bits
B2	244	72%	Acc	$73 \pm 1\%$	<i>62</i>	$87 \pm 1\%$	<i>72</i>	$87 \pm 1\%$	<i>70</i>	$80 \pm 2\%$		%
			Info	$0.02 \pm 0.02$	<i>0.00</i>	$0.30 \pm 0.02$	<i>0.00</i>	$0.28 \pm 0.02$	<i>0.00</i>	$0.13 \pm 0.03$	$-0.12$	Bits
C1	229	59%	Acc	$63 \pm 5\%$	<i>51</i>	$76 \pm 1\%$	<i>54</i>	$79 \pm 1\%$	<i>55</i>	$75 \pm 1\%$		%
			Info	$0.04 \pm 0.04$	<i>0.00</i>	$0.19 \pm 0.01$	<i>0.00</i>	$0.24 \pm 0.02$	<i>0.00</i>	$0.16 \pm 0.01$	$-0.38$	Bits
C2	188	70%	Acc	$71 \pm 2\%$	<i>59</i>	$85 \pm 2\%$	<i>70</i>	$89 \pm 2\%$	<i>68</i>	$82 \pm 1\%$		%
			Info	$0.03 \pm 0.03$	<i>0.00</i>	$0.30 \pm 0.04$	<i>0.00</i>	$0.37 \pm 0.06$	<i>0.00</i>	$0.19 \pm 0.03$	$-0.12$	Bits

Accuracy (Acc) and information (Info) rates of three different statistical classifiers (PDA, SVM, and LVQ) for all six datasets and one benchmark dataset are shown. For each dataset (labeled in the leftmost column), accuracy and information rates are each presented on a separate row (labeled in the rightmost column). Chance levels for each classifier are listed to the left of the results for each classifier in italics. For reference, the number of trials, the behavioral performance of the animal for each session, and the average predictive information for individual neurons within a particular dataset are listed in the first three columns. The redundancy for each dataset ( $P_{\text{Ensemble}}$ ) is listed in the last column.

predictive information from random data ( $I_{\text{Neuron}} > 0.016$ ) and that the mean predictive information of individual neurons in our data were twice this value.

Ensembles of neurons could be used to discriminate between conditioned and premature trials with an average accuracy of  $82.5 \pm 4.9\%$ . Accuracy for datasets with randomly permuted behavioral labels was  $61.7 \pm 8.1\%$ . Therefore, the improvement over chance levels of classification was  $>20\%$ . Ensembles encoded an average of  $0.16 \pm 0.06$  bits ( $I_{\text{Ensemble}}$ ) of predictive information with LVQ and as much as  $0.31 \pm 0.12$  bits of predictive

information with SVM (Table 3); that is, ensembles encoded from  $18 \pm 7\%$  [with LVQ (Table 3)] to  $34 \pm 13\%$  [with SVM (Table 3)] of the possible predictive information. Ensembles encoded significantly more predictive information than single neurons ( $t = 7.34$ ;  $p \ll 0.001$ ). Larger ensembles tended to encode more predictive information ( $R = 0.85$ ;  $p < 0.03$ ). Ensembles with pseudorandomly assigned behavioral labels provided  $0.004 \pm 0.005$  bits of predictive information, significantly less than ensembles with appropriately assigned behavioral labels ( $t = 6.64$ ;  $p \ll 0.001$ ).



**Figure 4.** The individual predictive information of neurons and their contributions to ensemble predictive information. The individual predictive information of each neuron (positive values,  $I_{\text{Neuron}}$ ) was plotted above the predictive information lost when that neuron is removed from the ensemble (negative values,  $I_{\text{Contrib}}$  or ensemble contribution) for all datasets (A1, A2, B1, B2, C1, and C2). Rasters of neurons from dataset A1 are shown in Figure 3. The 95% confidence level for chance is drawn as a light gray line at 0.016 bits.

Importantly, we performed all of the analysis above with multiple statistical classifiers in both WEKA and R. Results of analysis on ensemble data with three different statistical classifiers are presented in Table 3. Although some classifiers (i.e., SVM) performed better than others (i.e., LVQ), all statistical classifiers indicated that the ensembles had significantly higher predictive information than random data ( $t = 6.12$ ;  $p \ll 0.001$ ) and had significantly higher predictive information than single neurons ( $t = 8.98$ ;  $p \ll 0.001$ ). Across datasets, information values calculated by different statistical classifiers were correlated for ensembles (LVQ vs SVM,  $R = 0.92$ ; SVM vs PDA,  $R = 0.53$ ; PDA vs LVQ,  $R = 0.59$ ) and for individual neurons (LVQ vs SVM,  $R = 0.80$ ; SVM vs PDA,  $R = 0.60$ ; PDA vs LVQ,  $R = 0.69$ ). Additionally, redundancy values of different classifiers were highly correlated (LVQ vs SVM,  $R = 0.94$ ; SVM vs PDA,  $R = 0.76$ ; PDA vs LVQ,  $R = 0.88$ ). These results indicate that the different statistical classifiers used in this study generated primarily convergent estimates of predictive information and redundancy.

### Single neurons contribute redundant information

To estimate the contributions of individual neurons to an ensemble ( $I_{\text{Contrib}}$ ), we calculated how much predictive information was lost when a neuron was removed from all ensembles in which a neuron might participate (see Materials and Methods) (Table 1). Removing a single neuron from an ensemble resulted in an average decrease in predictive information of  $0.016 \pm 0.05$  bits ( $\hat{I}_{\text{Contrib}}$ ). Importantly,  $I_{\text{Contrib}}$  for 87% of neurons (68 of 78) statistically included zero (Fig. 4, note large error bars for  $I_{\text{Contrib}}$ ), indicating that removing a neuron from an ensemble often did not greatly change the predictive information of the ensemble.

We found that information lost with neuron removal was significantly less than the information provided by the neurons themselves (i.e.,  $I_{\text{Contrib}} < I_{\text{Neuron}}$ ; paired  $t = 4.32$ ;  $p \ll 0.001$ ), and there was no obvious relationship between these informational values ( $R = 0.11$ ;  $p < 0.17$ ) (Fig. 4). These results suggest that the information contributed by single neurons to the ensembles was not independent.

To determine whether interactions between the neurons were synergistic or redundant, we calculated  $P_{\text{Neuron}}$  according to Equation 3 for each neuron in each ensemble. The average value of  $P_{\text{Neuron}}$  for all neurons was  $-0.016 \pm 0.03$  bits, which suggests

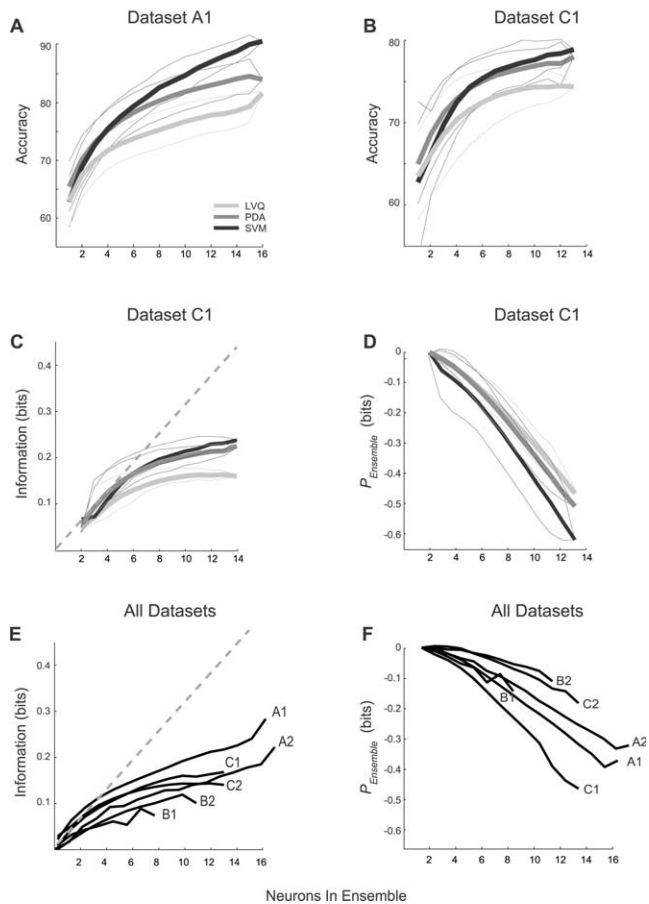
average redundancy. Most neurons contributed redundant information to the ensembles (43 of 45 neurons, or 96%, of neurons with significant information were redundant). Only neurons 1 and 6 in dataset B1 (2 of 45 neurons, or 4% of neurons with significant information) had synergistic ensemble interactions.

Because individual neurons encoded a small fraction of the possible information ( $4 \pm 3\%$ ), redundant information contributed by individual neurons was unlikely to be a result of information saturation by high information rates of individual neurons; that is, if a few neurons were highly informative, any additional neurons would by definition provide redundant information. In our data, we found that the removal of highly informative neurons did not greatly impact ensemble performance (Fig. 4, neuron 8 in dataset A1, neurons 3 and 8 in dataset C1), once again suggesting redundant interactions between neurons at the ensemble level.

### Neuronal ensembles are highly redundant

To determine whether ensembles as a whole were redundant or synergistic, we calculated the value  $P_{\text{Ensemble}}$  according to Equation 4, which represents the difference between the predictive information of an ensemble and the sum of the predictive information of the component neurons. All six ensembles were redundant ( $\hat{P}_{\text{Ensemble}} = -0.24 \pm 0.14$  bits) (Table 3).

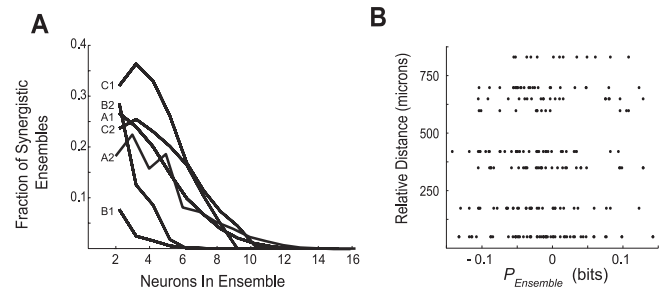
A redundant ensemble should maintain performance as it is degraded. To test this property, we progressively removed neuronal data from each ensemble and estimated accuracy and predictive information. Data from all animals suggested that, regardless of classifier, accuracy of prediction decreased slowly as neurons were removed when ensembles were larger than a few neurons and decreased rapidly as neurons were removed when ensembles were small (Fig. 5A,B). Predictive information increased much less slowly than would be predicted with an independent coding scheme (in which each neuron encoded an average of 0.034 bits) (Fig. 5C,E). As neurons were excluded, the remaining ensembles maintained accuracy (across datasets,  $80 \pm 12\%$  of ensemble information was maintained with only 50% of neurons) (Fig. 5A,B). However, predictive information declined rapidly after  $<30\%$  of the neurons remained in the ensemble (Fig. 5C,E). For small ensembles of neurons, the average value of  $P_{\text{Ensemble}}$  was near zero (e.g.,  $0.006 \pm 0.012$  for pairs) (Fig. 5D,F).



**Figure 5.** Analysis of ensemble predictive information as neurons are added/removed reveals high levels of redundancy. Accuracy of ensemble prediction as a function of the number of neurons for dataset A1 (**A**) and for dataset C1 (**B**), as quantified by three different statistical classifiers (SVM, PDA, and LVQ) for all possible combinations of neurons. SD plotted as lighter lines. **C**, Predictive information as a function of the number of neurons in the ensemble for dataset C1 with three different statistical classifiers (SVM, PDA, and LVQ; colors as in **A**). The dotted gray line represents the increase in predictive information that would be expected from an independent coding scheme if each neuron encoded an average of 0.034 bits, the average predictive information for individual neurons in our datasets. Compare with Figure 2. **D**,  $P_{\text{Ensemble}}$  as a function of the number of neurons in the ensemble for dataset C1 with three different statistical classifiers (SVM, PDA, and LVQ; colors as in **A**). **E**, Predictive information as a function of the number of neurons in the ensemble for all datasets; datasets are labeled on the figure. **F**,  $P_{\text{Ensemble}}$  as a function of the number of neurons in the ensemble for all datasets; datasets are labeled on the figure.

For larger ensembles,  $P_{\text{Ensemble}}$  became more negative (e.g.,  $-0.13 \pm 0.07$  for 8 neuron ensembles) (Fig. 5D,F), signifying a net increase in redundancy across datasets ( $t = 3.67$ ;  $p < 0.006$ ) with an increase in ensemble size across datasets.

Across our datasets, we found that  $P_{\text{Ensemble}}$  was indeed negatively correlated with predictive information (mean  $R = -0.78$ ;  $p \ll 0.001$  with exponentially transformed predictive information) (Fig. 5E). We also found that  $P_{\text{Ensemble}}$  was negatively correlated with the number of neurons in the ensemble (across datasets, mean  $R = -0.85 \pm 0.02$ ;  $p \ll 0.001$ ) (Fig. 5F). A multiple linear regression revealed that 73% of the variance of  $P_{\text{Ensemble}}$  was explained by predictive information and ensemble size ( $R^2$  of ensemble size = 0.45,  $R^2$  of exponentially transformed predictive information = 0.28;  $R^2 = 0.73$ ;  $F_{\text{model}} = 209$ ;  $p \ll 0.001$ ). These data indicate that redundancy increases (i.e.,  $P_{\text{Ensemble}}$  becomes more negative) as a function of both predictive information and ensemble size.



**Figure 6.** Synergy among ensemble data. **A**, Fraction of synergistic ensembles as a function of number of neurons in ensembles. **B**,  $P_{\text{Ensemble}}$  for pairs of neurons plotted against distance between microelectrodes from which neurons were recorded.

Finally, we investigated whether the redundancy we observed was a result of a “ceiling effect,” i.e., a saturation of predictive information attributable to similarities in neuronal response properties (Rolls et al., 1997). This effect is unlikely for three reasons. First, individual neurons provided little predictive information (i.e.,  $4 \pm 3\%$ ). Second, removing any particular neuron had a small effect on ensemble predictive information (Figs. 4, 5). Third, trial shuffling (i.e., randomizing the trial orders within each trial type for individual neurons) significantly increased ensemble predictive information across datasets (increase in accuracy,  $3.5 \pm 1.9\%$ ; paired  $t = 4.6$ ;  $p < 0.006$ ).

### Redundancy and synergy

Our experimental data revealed redundant interactions within large ensembles of weakly coding neurons. However, in our data from the rat motor cortex, we found that small ensembles (less than six neurons) exhibited rapid increases in predictive information as neurons were added to the ensembles (Fig. 5C,E). This data suggested a nonredundant coding scheme (Fig. 2), such as synergy. To assess the extent of synergy in our data, we plotted the percentage of significant synergistic ensembles as a function of the ensemble size and found that the fraction of significant synergistic interactions was inversely related to the number of neurons in the ensemble (Fig. 6A). Significance levels were determined by calculating  $P_{\text{Ensemble}}$  for 1000 two-neuron ensembles with randomly permuted behavioral labels. The 95% confidence interval for  $P_{\text{Ensemble}}$  was between 0.016 and  $-0.032$ . We interpreted  $P_{\text{Ensemble}}$  values outside this range to be significant. We found declining synergy with increasing ensemble size in every dataset and with every statistical classifier we used, although some statistical classifiers found higher levels of synergy (i.e., SVM) than others (i.e., LVQ).

Finally, we examined whether there were any spatial determinants for synergistic or redundant neuronal interactions. We determined the distance between each neuron across the microelectrode arrays used for the neuronal recordings and plotted those distances against  $P_{\text{Ensemble}}$  for pairs of neurons. We observed no obvious relationship between  $P_{\text{Ensemble}}$  and the distance between electrodes from which neurons were recorded ( $R = 0.08$ ;  $p < 0.12$ ) (Fig. 6B).

### Discussion

We studied how interactions among neuronal ensembles in the rat motor cortex influence predictions of behavioral performance in a simple reaction time task. We used statistical pattern recognition methods to quantify predictive information conveyed by single neurons and groups of neurons of varying complexity. Using a cluster of computer workstations, we were able to ac-

count for interactions between all possible combinations of neurons (involving many thousands of combinations; Table 2), something that, to our knowledge, has not been accomplished previously. We report three main findings. First, the predictive information conveyed by single cortical neurons is not related to the contribution that neuron makes to information conveyed by neuronal ensemble. Second, ensembles of cortical neurons tend to be highly redundant. Finally, although large ensembles are highly redundant, significant synergistic interactions exist in smaller ensembles.

### Motor cortex and simple reaction time tasks

In this study, spike trains were collected from chronically implanted arrays of electrodes in rat motor cortex during performance of a simple reaction time task with a variable foreperiod. In such a task, there is an increasing likelihood that the trigger stimulus will occur as time passes during the foreperiod (Naa-tanen, 1970). Prompt reaction times are thought to depend on processes of time estimation and stimulus detection that converge on a “response generator,” e.g., motor cortex (Ollman and Billington, 1972; Kornblum, 1973). The motor cortex should thus be responsive to temporal and sensory factors during the foreperiod. However, processes related to stimulus detection should only occur on trials with conditioned (correct) responses. There are several large-scale brain potentials that become active during the foreperiod of simple reaction time tasks (for review, see Brunia, 1999). One of them, the contingent negative variation (CNV), is evoked by the trigger stimulus. If rats are capable of generating this potential (Pirch, 1980), then a CNV-like process would differentiate neuronal processing on the two types of trials examined in this study. The lack of activation of motor cortex by a CNV-like process may have resulted in reduced levels of excitability in motor cortex, as is apparent in the perievent histograms in Figure 3. This effect might also result in quantitative differences in neuronal ensemble level activity on conditioned and premature responses, and these effects might be manifest in redundant interactions among neurons.

The shortest observed RTs may represent anticipatory responses initiated before the trigger stimulus. If neuronal stimulus relationships were different on such anticipatory trials, then removing such trials should improve classification of conditioned versus premature trials. However, when we removed trials with very short reaction times, we observed equivalent or slightly decreased classification of the remaining conditioned responses versus premature responses (data not shown). These results suggest that motor cortex was influenced more by the absence of the trigger stimulus than by anticipatory responses on the premature response trials.

### Functional interpretation of synergy and redundancy

Our results suggest that single neurons in the rat motor cortex do not function as independent encoders of behavioral performance in a simple reaction time task. Instead, the neurons are highly redundant. As was pointed out by Meijers and Eijkman (1974), redundancy may exist in the motor cortex to overcome the large amount of variability in the onset latencies of corticospinal neurons (Evarts, 1966) relative to onset latencies in muscle (Botwinick and Thompson, 1966). Redundancy might also be attributable to activations of functionally related groups of muscles (Donoghue et al., 1992; Plautz et al., 2000; Holdefer and Miller, 2002; Jackson et al., 2003; Kargo and Nitz, 2003; Morrow and Miller, 2003) that are used to control the response lever and maintain the rat's posture during the trial. Redundancy in motor

cortex would allow for increased efficiency in controlling functionally related sets of muscles (Barlow, 2001), or, more practically, to changes that are known to occur with motor skill learning in which accessory muscles tend to change with learning more than primary mover muscles (Heise, 1995). Indeed, increases in correlated firing in motor cortex, an indirect measure of redundant processing, have been reported recently to accompany the learning of sensorimotor tasks (Gemba and Sasaki, 1984, 1988; Laubach et al., 2000; Cohen and Nicolelis, 2004; Kargo and Nitz, 2004; Paz and Vaadia, 2004). More generally, the advantages of redundancy in cortical neurons may offset the advantages of channel capacity reduction (Shannon and Weaver, 1949) and economy of energy (Allman, 1990) because of greatly enhanced signal-to-noise during goal-oriented behavior (Barlow, 2001).

### Distributed coding in neuronal ensembles

Distributed coding has been examined in a relatively small number of studies. Humphrey et al. (1970) found that small sets of neurons could accurately predict several motor variables. More recently, Wessberg et al. (2000) performed a similar analysis in ensembles with hundreds of neurons in multiple parts of primate cortex to predict hand position during two- and three-dimensional arm movement tasks and found that ensembles performed at high levels (prediction above 90% of the variance of hand trajectory) despite removal of up to one-third of the neurons in the ensemble. Similarly, Averbeck et al. (2003) found evidence for high levels of redundancy while recording from ensembles up to 22 neurons in primate prefrontal cortex during a shape-copying task. In the rat primary somatosensory cortex, Ghazanfar et al. (2000) found graceful degradation of cortical ensembles when discriminating among sites of stimulation on the whisker pad. These results are consistent with our results and further suggest that redundancy is a major factor in information processing in multiple cortical systems.

Studies that have investigated how small cortical ensembles work together to encode information have found less redundancy than reported here. Gawne and Richmond (1993) studied responses of pairs of neurons in the inferior temporal cortex to complex visual stimuli and found that 20% of all pairwise neuronal interactions were redundant. Rolls et al. (2004) report lower levels of redundancy (4–10%) in inferior temporal cortex when discriminating between 20 faces. In the primate motor cortex, Maynard et al. (1999) found only ~20% of all pairwise neuronal interactions were redundant in the motor cortex during directional limb movements, whereas the remainder were synergistic. Reich et al. (2001) found entirely independent interactions between small ensembles (less than six neurons) of simultaneously recorded neurons in primary visual cortex. Samonds et al. (2004) found high levels of synergy for small ensembles (up to six neurons) when recording from cat V1 while a drifting sinusoidal grating was presented.

In contrast, in the present study, we found that most ( $99.3 \pm 0.01\%$ ) of large ensembles (more than eight neurons) are entirely redundant. However, just  $36 \pm 12\%$  of neuron pairs were redundant, with  $23 \pm 9\%$  exhibiting synergistic interactions (the remainder of pairs did not exhibit significant synergy or redundancy). One explanation for the high redundancy we find is that larger ensembles may mask synergy present in smaller ensembles. Thus, the low levels of redundancy observed in small ensembles in previous studies (Gawne and Richmond, 1993; Maynard et al., 1999; Reich et al., 2001; Rolls et al., 2004; Samonds et al., 2004; Purushothaman and Bradley, 2005) are entirely compatible with our results, because we find little redundancy in small ensembles.



An alternative explanation, however, is that the sensory mapping studies above used many classes of stimuli, whereas our study had just two outcomes of task performance. This issue will require additional experimental studies to be resolved.

### Limitations of the statistical pattern recognition approach

Our estimates of mutual information depend to some extent on the specific algorithm used for classification. As a result, our estimates may underestimate limits on mutual information for encoding behavioral performance (see Materials and Methods). Furthermore, we calculated synergy and redundancy based on estimates generated by statistical classifiers. It is possible that the classifiers have sources of bias that direct estimates of mutual information would avoid (see Materials and Methods) (Schneidman et al., 2003). We used different classifiers on benchmark data and random neuronal data to examine this issue. However, we cannot rule out bias in our measures of  $P_{\text{Ensemble}}$  because we know of no practical method to directly measure mutual information for large ensembles of neurons. Despite these concerns, we believe that our approach is a feasible way to analyze interactions among ensembles of neurons. The high levels of redundancy we found in all datasets using multiple statistical classifiers lends confidence to our interpretation. We hope that future studies will consider these issues. However, we believe the ultimate test of the value of synergistic and redundant neuronal interactions for encoding behaviorally relevant information will be through experiments, perhaps involving real-time analyses of spike trains recorded in awake, behaving animals (Humphrey et al., 1970; Wessberg et al., 2000; Serruya et al., 2002; Taylor et al., 2002; Ben-Shaul et al., 2003; Carmena et al., 2003; Lebedev et al., 2004).

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