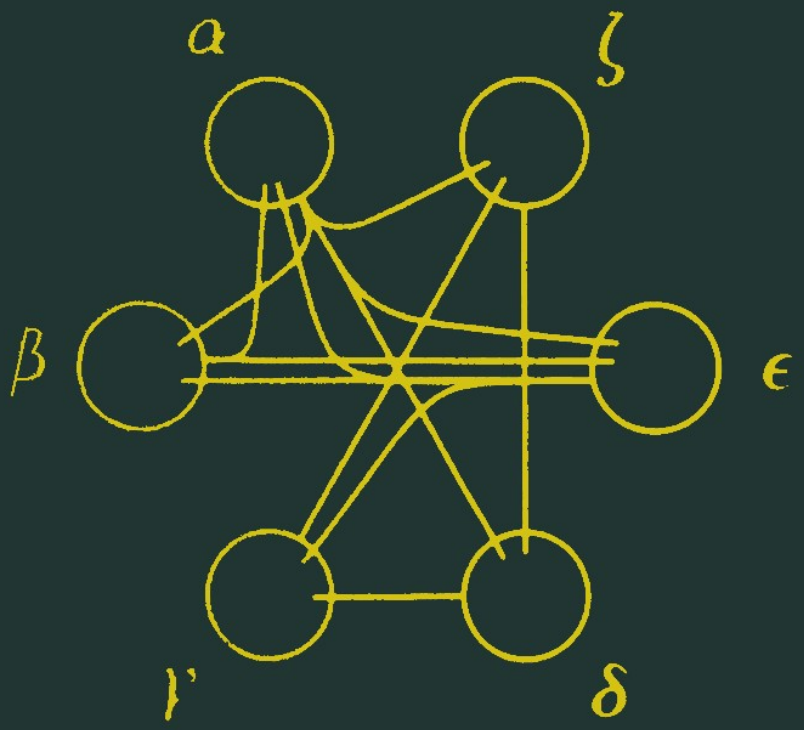
A. Aertsen V. Braitenberg (Eds.)

Information Processing in the Cortex

Experiments and Theory



Springer-Verlag


ALLE ZEIT WACH
1842

Ad Aertsen Valentino Braitenberg (Eds.)

Information Processing in the Cortex

Experiments and Theory

With 102 Figures

Springer-Verlag
Berlin Heidelberg New York
London Paris Tokyo
Hong Kong Barcelona Budapest

Dr. Ad Aertsen
Universität Bochum
Institut für Neuroinformatik
Postfach 102148
Gebäude ND 04
W-4630 Bochum, FRG

Professor Dr. Valentino Braitenberg
Max-Planck-Institut
für biologische Kybernetik
Spemannstraße 38
W-7400 Tübingen, FRG

ISBN 978-3-642-49969-2 ISBN 978-3-642-49967-8 (eBook)
DOI 10.1007/978-3-642-49967-8

Library of Congress Cataloging-in-Publication Data.
Information processing in the cortex: experiments and theory / edited by Ad Aertsen and Valentino Braitenberg. p. cm. Includes bibliographical references and index.
ISBN 978-3-642-49969-2 (U.S.)
1. Cerebral cortex. 2. Human information processing. 3. Cognitive neuroscience. I. Aertsen, Ad (Adrianus), 1948–. II. Braitenberg, Valentino. QP383.I54 1992 612.8'25–dc20 92-19742 CIP

Typesetting: Camera ready by Margarete Ghasroldashti, MPI, Tübingen
31/3145-5 4 3 2 1 0 – Printed on acid-free paper

Coding and Computation in the Cortex: Single-Neuron Activity and Cooperative Phenomena

Eilon Vaadia[1] and Ad Aertsen[1,2,3]

[1] Dept. of Physiology, Hadassah Medical School, P.O. Box 1172, Hebrew University, Jerusalem, Israel
[2] Max-Planck-Institut für biologische Kybernetik, Spemannstrasse 38, 7400 Tübingen, Germany

Introduction

There is widespread consensus among neurophysiologists and neuropsychologists that neurons are involved in information processing and computations carried out by the brain. Yet there is still remarkably little understanding of the mechanisms underlying these processes. Similarly, also the nature of the neural code (or codes) being used by the brain is still very much open for discussion. In view of this, it is essential to consider different alternatives. Not only does each of them dictate a way of thinking about brain mechanisms, they also suggest different experimental approaches toward experimental studies of these mechanisms.

A common view among many neurobiologists suggests that the basic element of the neural code resides in the spike activity of a single neuron. A different view was first presented by Hebb (1949), who suggested that the coherent activity within groups of neurons ('cell-assemblies') is the basis of the neural code. In this paper we will present results from an ongoing electrophysiological study of cortical function, focussing on different aspects of coding and processing revealed by recordings of single and multiple neuron activity. We will illustrate our considerations by experimental results from different cortical areas in anaesthetized, as well as in awake, behaving monkeys.

---

[3] present address: Institut für Neuroinformatik, Ruhr-Universität, P.O. Box 102 148, 4630 Bochum, Germany

Cortical activity at the level of single-neuron spike trains

Single-neuron firing rate as a neural code

It is generally assumed, at least implicitly, that the most relevant parameter to be extracted from the spike train is the rate of spike occurrence, the single-neuron firing rate. Barlow (1972) suggested that, "The frequency of neural impulses codes subjective certainty: a high impulse frequency in a given neuron corresponds to a high degree of confidence that the cause of the percept is present in the external world." (See also Barlow's contributions to this Volume.) Thus, according to this view, the neural code is the firing rate of a single neuron and the appropriate experimental tool is a microelectrode that can isolate and record the activity of a single neuron ('single-unit activity').

Indeed, single-unit studies in many cortical and sub-cortical areas have clearly demonstrated highly specific changes of firing rates that were related to sensory and/or motor processing. Amongst others, this culminated in a wealth of data on 'receptive field' properties of neurons in various parts of the sensory system, exemplified in the work of Mountcastle (1957, 1977) and Hubel and Wiesel (1968, 1977). In addition, however, this approach also turned out to be fruitful in the study of cognitive and other higher brain functions, such as perceptual analysis of sensory input, selective attention, short-term memory, etc. (Fuster 1973, 1989; Evarts et al. 1984; Perrett et al. 1982; Goldberg and Segraves 1987; Goldman-Rakic 1987; Niki and Watanabe 1976, 1979; Gottlieb et al. 1989).

An example which illustrates how specific aspects of higher cortical function may be expressed in the firing rate of a single neuron is presented in Figure 1 (from Vaadia et al. 1986). It shows the responses of a neuron in the frontal cortex of a monkey which was trained to respond to acoustic or visual stimuli, presented at one of 5 possible locations. In one paradigm the monkey had to touch a key at the location of the stimulus. There were two such 'localizing' tasks: *auditory localization (AL)* and *visual localization (VL)*. In addition, the same monkey was also trained to perform an *auditory detection (AD)* paradigm. In this 'detection' task, one of the 5 keys was randomly designated as a 'detect key' and the monkey had to touch this key, irrespective of the stimulus location, until a new 'detect key' was designated. The VL, AL, and AD conditions were alternated in blocks of 20 trials. In each block of AD trials, a different key was designated as

the 'detect key'. This latter task was designed to produce hand and eye movements during the detect task that were similar to those employed by the monkey in the AL and VL conditions (for details on the task and additional control conditions, see Vaadia et al. 1986). Five groups of five histograms each are shown. The first row shows that the neuron did not respond to auditory stimuli when the monkey was not performing any behavioral task (non-performing condition: NP). The second (AD(S)) and third (AD(R)) rows show that the neuron did not respond to stimuli (AD(S)) in the 'auditory detect' condition, nor was it

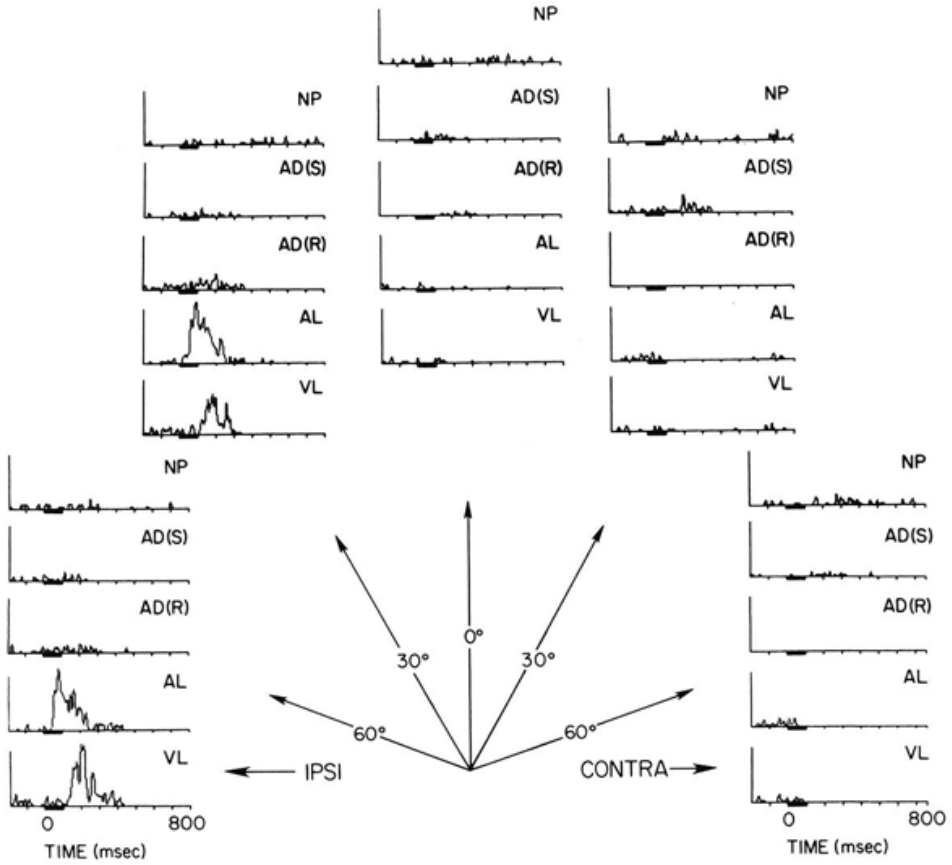


Fig. 1. PST histograms showing the activity of one neuron as a function of stimulus location in 5 behavioral conditions. *NP*: non-performing conditions (stimuli: noise bursts of 100 ms). *AD*: responses during performance of the auditory detection task, with *AD(S)*: histograms of the responses, sorted according to the location of the stimulus, *AD(R)*: histograms of the responses sorted according to the directional location of the arm movement. *AL*: responses of the unit when the monkey had to localize auditory stimuli. *VL*: responses of the neuron when the monkey had to localize visual stimuli. (From Vaadia et al. 1986)

activated in relation to arm movements that were made towards the targets (AD(R)). However, the last two rows reveal that a clear response to stimuli from 60 and 30 degrees at the ipsilateral side (irrespective of their modality) was evoked when the monkey had to localize the stimuli (AL, VL).

The responses of the neuron demonstrated in this Figure were not related strictly to auditory or visual stimuli, nor were they related to movements per se. The neuron was activated only when the location of the stimulus, irrespective of its modality, served as a cue for the appropriate behavioral response. It was therefore suggested that this neuron was involved in a mechanism that extracts spatial cues from at least two modalities.

Under appropriate behavioral conditions, prolonged slow waves of activity, marking distinct perceptual, cognitive and linguistic processes, and lasting hundreds of milliseconds to several seconds, can be recorded in a single cortical area (Donchin 1984; Deeke et al. 1985; see also the contributions by Elbert and by Arieli in this Volume). Signs of such long processing could also be found in the activity of single neurons recorded from sensory, association, premotor and motor cortices of behaving monkeys during some specified stages of behavior (Fuster 1989; Wise and Mauritz 1985; Gottlieb et al. 1989; Vaadia et al. 1989). An example from such studies is shown in Figure 2 (from Gottlieb et al. 1989). This Figure illustrates the behavior of the firing rate of a single neuron in the auditory cortex of a monkey, trained to perform an auditory short-term memory task. Two tone bursts (S1 and S2), separated by a silent inter-stimulus interval of 1 second, were presented in each trial. The monkey had to touch one key if the tones were identical, and another one if they were different. The firing rate of the unit while the monkey was performing correctly is shown as the solid line. The broken line shows the activity of the same single unit when the water spout was removed and the monkey did not perform the task.

Though it is not possible to tell from such an experiment how this particular unit was engaged in forming the short-term memory of pitch, it is clear that the neuron did not end its role when the stimulus was turned off. On the contrary, Figure 2 clearly shows that the neuron took part in, or was affected by, a prolonged process that took place in the primary auditory cortex during the inter-stimulus interval, persisting long after the information was presumably transmitted to other cortical areas. Approximately 60% of the recorded neurons in

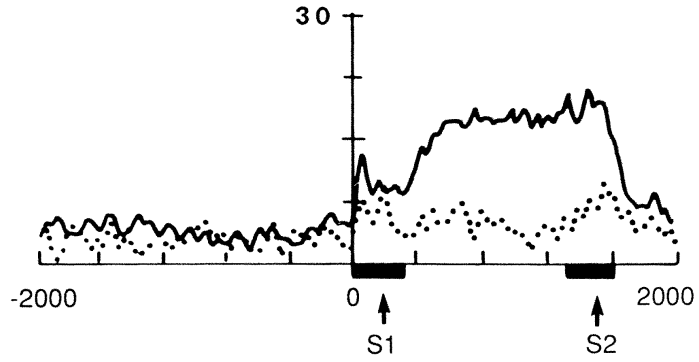


Fig. 2. Activity of a single neuron in the auditory cortex of the Rhesus monkey. The solid line shows a PST-histogram, collected during performance of the short-term memory task. The broken line shows the PST-histogram, collected when the stimuli were presented but the monkey did not perform the task. The abscissa describes the time from 2.0 sec before onset of the first stimulus (*S1*) until 0.45 sec after the second stimulus (*S2*) ended. The ordinate describes the firing rate in spikes/sec. (Adapted from Gottlieb et al. 1989)

this study showed such prolonged changes in their firing rates during the interval between the two tones (Gottlieb et al. 1989).

The activity of a single neuron may be quite complex. An example of this is given in Figure 3. It shows a raster-display and PST-histogram, illustrating the activity of a neuron in the premotor cortex of a monkey, recorded during performance of a stimulus-guided reaching task (after Vaadia et al. 1988). The monkey initiated a trial ('INIT') by touching a key (located in front of him in a mid-sagital location) and waited for 6 seconds. Then, one of two keys (either on the left or on the right) was illuminated (the 'cue', marked as 'Q' in Fig. 3). The monkey had to maintain contact with the center key for an additional 500 msec and then touch the illuminated key. Three components of activity can be seen in the PST-histogram. First, the unit was activated during the waiting period (from INIT to CUE, starting about 3 sec before cue onset). EMG recordings of superficial muscles indicated that the monkey did not attempt to make movements during the pre-cue interval. This and other considerations led to the suggestion that this activity was not related to the preparation or execution of the movements, but rather to other aspects of task performance, such as expectation or timing of events (Vaadia et al. 1988). Subsequently, the spike discharge of the unit was suppressed in response to the directional-cue onset and, finally, it was activated again later at the time of

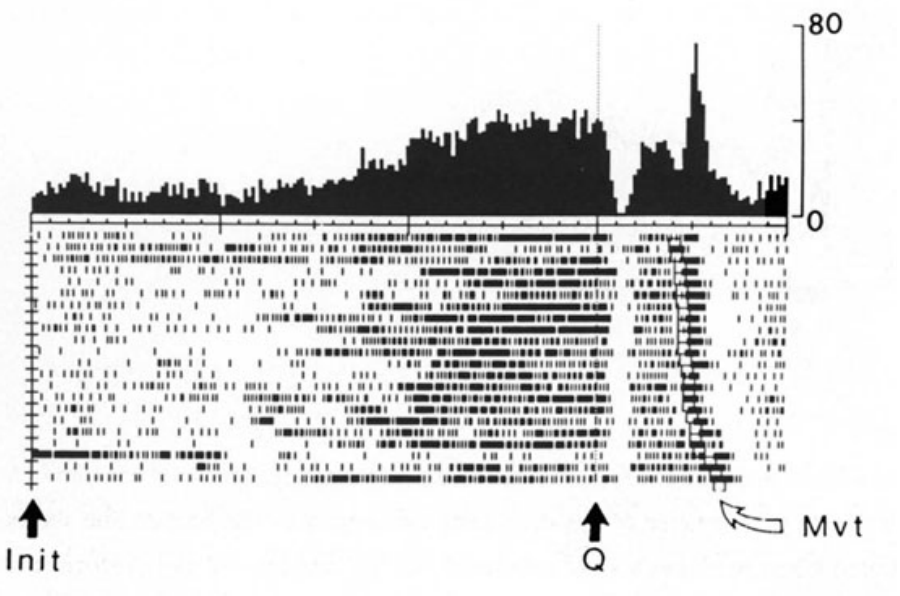


Fig. 3. Activity of a single neuron in the premotor cortex of the Rhesus monkey. The raster display and PST-histogram show 8 sec of activity centered around the onset time of the spatial cue (*Q*). Trial initiation (*INIT*) is marked by a plus sign on each raster. The beginning of the limb movement (*MVT*) is marked by an empty square. (From Vaadia et al. 1988)

movement onset (marked by an empty square on each line of the raster display). This last component of activity was direction-specific and could be easily matched with some of the EMG records, suggesting that it was related to motor function. As this result illustrates, this type of complex activation pattern strongly suggests a single neuron is not dedicated to the processing of just one single function.

Summarizing, the notion that the rate of single-neuron firing may serve as a neural code is supported by the above findings. Nevertheless, these findings do no tell us what the mechanism is by which the bi-modal responses (cf. Fig. 1) or the prolonged (cf. Fig. 2) and complex (cf. Fig. 3) rate modulation patterns were generated. Moreover, these findings do not rule out the possibility that increased firing rate may not be the sole encoding mechanism, or may even be a by-product of other mechanisms. Finally, there is a conceptual problem. If we accept the notion of firing rate as the sole basis of neural encoding, this implies that a neuron carries information only whenever its rate is elevated, but that all other spikes, the so-called 'background' activity, do not. It turns out, however, that the probability of finding a cortical neuron with an elevated firing rate is extremely low: the average cortical neuron spends over 99.8% of its time being idle (Abeles et al.

1990). This, evidently, makes it rather unlikely that single-neuron firing rate serves as the sole mechanism for neural encoding in the cortex. We conclude that it is important to also examine alternative codes.

Single-neuron firing patterns as a neural code

It is quite conceivable that a neuron may be coding for something (be it as a 'grandmother' neuron, or as a member of a functional group) without any observable change in its firing rate. One such possibility of an alternative code resides in the temporal firing pattern of the neuron. We present here two examples to demonstrate the feasibility of such a single-neuron firing pattern code, one taken from the somatosensory cortex, the other from the auditory cortex. For other examples of single-unit firing patterns as a potential neural code we refer to Dayhoff and Gerstein 1983a,b; Abeles 1983; and Abeles al. 1983.

An example which demonstrates the effect of stimuli on the firing pattern of single cortical neurons is shown in Figure 4. This result was taken from a study by Ahissar and Vaadia (1990), who examined properties of oscillatory neurons in the upper bank of the lateral sulcus (a polisensory area, were many neurons responded to tactile stimuli) of an awake, behaving monkey. The Figure shows the effect of two different tactile stimuli on the firing patterns of two simultaneously recorded neurons. Both neurons (4 and 6) showed clear oscillatory patterns when no stimuli were applied ('spontaneous activity' (SP1-3)), which could be suppressed by tactile stimuli (STIM1: soft strokes of the contralateral small toes at 1 stimulus/second, and STIM2: soft strokes of the contralateral big toe at 1 stimulus/second). The Figure further illustrates that tactile stimuli had different effects on the mean firing rates and on the temporal firing patterns of the two neurons. For example, the oscillatory firing pattern of unit 4 was suppressed by both STIM1 and STIM2, whereas only STIM1 affected the firing rate, which was enhanced in this case. For unit 6, on the other hand, again both STIM1 and STIM2 suppressed the oscillatory firing pattern, but now the firing rate was only affected (i.e. enhanced) by STIM2. It was further reported that in most of the cases no consistent relations were found between the effects of stimuli on a neuron's firing rate and their effects on its oscillatory firing pattern. In none of the cases could a significant cross-correlation be observed between any of the pairs of

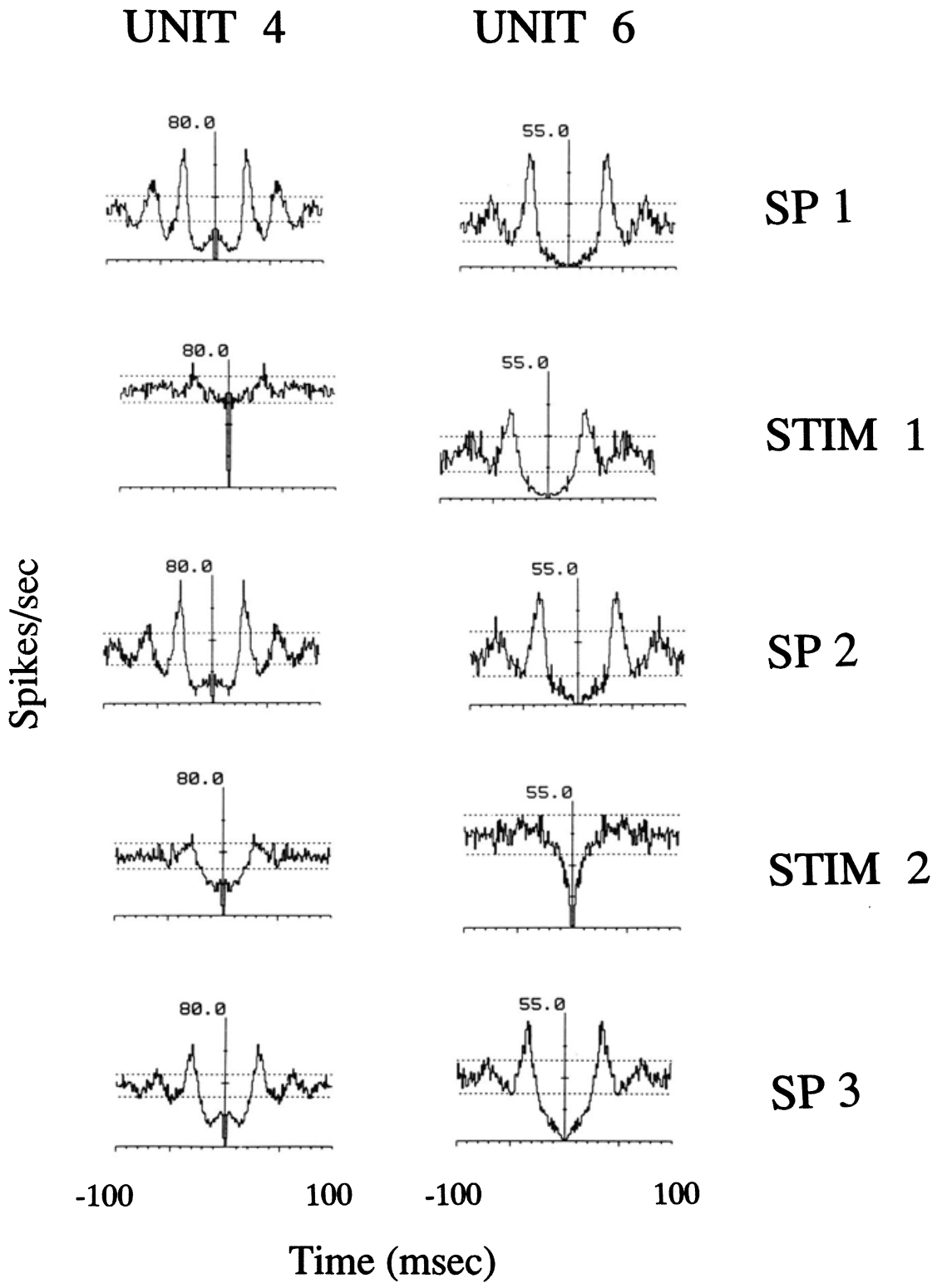


Fig. 4. Suppression of oscillatory activity in the somatosensory cortex of a monkey by tactile stimuli. (Left) Neuron 4 (33 Hz, full scale: 80 spikes/s). (Right) Neuron 6 (27 Hz, full scale: 55 spikes/s). Five consecutive periods are shown. SP-1, 131 s of spontaneous activity; the oscillatory activity is clearly seen. STIM-1, 147 s of soft strokes (1/s) to the contralateral small toes; the oscillations of unit 4 were suppressed and its averaged firing rate was elevated from 32 to 62 spikes/s; the firing rate of unit 6

oscillating neurons, not even when they were recorded on a single microelectrode.

In contrast to the oscillatory firing patterns in the upper banks of the lateral sulcus, the most striking feature of firing patterns of single neurons in the auditory cortex of monkeys and cats was the absence of periodicities (e.g. Abeles 1982a; Vaadia and Abeles 1987; Gottlieb et al. 1989; Ahissar et al. 1992). Nevertheless, in some cases it was found that the firing pattern was clearly affected by the behavioral state, even though the average firing rate remained almost the same. An example of this is given in Figure 5, which shows two 'snowflake' displays, mapping the timing of triplets of spikes. Each triplet is defined by two intervals T_B-T_A and T_C-T_B, where T_A, T_B and T_C are the times of occurrence of the spikes A, B and C. A triangular coordinate system is used to map the triplets into unique points in a hexagon. For example, a bin which maps the cases where the spike C occurred 100 msec after spike B, and the spike B occurred 50 msec after spike A, lies at the point where the vertical line, perpendicular to the upper-left axis (T_B-T_A) at +50 msec meets the line perpendicular to the lower-left axis (T_C-T_B) at +100 msec. (For more details on 'snowflake' display see Perkel et al. 1975 and Abeles 1982a). In this particular example, all spikes were taken from a single spike train. Therefore, the snowflakes represent the three-spike auto-correlation of the neuron: each triplet of spikes is represented in three bins, and the displays are symmetric in a triangular fashion.

By computing such 'snowflake' displays for different sections of recorded activity, we can observe changes in the neuronal activity and, in particular, extract the temporal patterns of spike triplets which dominated during each of these sections. The two snowflakes in Figure 5 represent the activity of a single neuron in the auditory cortex of a monkey, recorded during each of two behavioral paradigms in an

---

was not affected and its oscillations were affected only very slightly. SP-2, 90 s of spontaneous activity; note the recovery of unit 4's oscillations. STIM-2, 117 s of soft strokes (1/s) to the contralateral big toe; the oscillations of the two neurons were suppressed; while the firing rate of unit 6 increased from 22 to 40 spikes/s, the firing rate of unit 4 was not affected. SP-3, 136 s of spontaneous activity; the oscillations recovered again. Recording of the two neurons lasted while the procedure (SP-1, STIM-1, SP-2, STIM-2, SP-3) was repeated seven times with similar results. In three sets, the procedure was carried out under ketalar anesthesia. (From Ahissar and Vaadia 1990)

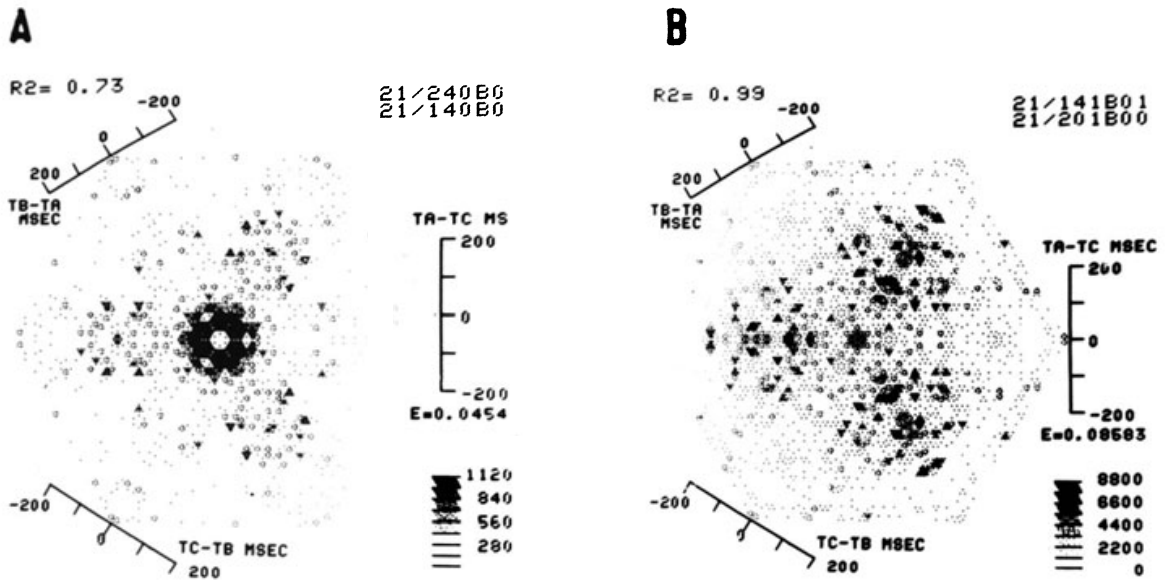


Fig. 5. Modification of single-neuron firing pattern by behavioral state. The hexagons in **A** and **B** show firing patterns of a single neuron in the auditory cortex of a monkey, recorded during each of two behavioral paradigms in an auditory discrimination task. The rate of firing is grouped to eight grey levels. The scale at the lower right marks these levels in percent of the expected rate. **A**: Three-spike auto-correlation, computed from the firing of the neuron during performance of the behavioral paradigm 1, where tone stimuli initiated right shifts of the lever. **B**: similar auto-correlation for the same neuron, computed from the firing during performance of the behavioral paradigm 2, where tone stimuli initiated left shifts of the lever. R_2 = mean firing rate; E = expected number of counts in each triangular bin. (From Vaadia and Abeles 1987).

auditory discrimination-reversal task (from Vaadia and Abeles 1987). In the first behavioral paradigm, presentation of a tone burst stimulus was associated with shifting a lever to the right, while presentation of a noise burst was associated with shifting the lever to the left. In the second paradigm, which was regularly alternated with the first, the contingencies were reversed: left shift after tone burst and right shift after noise burst. Fig. 5A shows the unit activity upon presentation of a tone stimulus during performance of the first behavioral paradigm, while Fig. 5B shows the same neuron's response to the same tone stimulus during the second paradigm. A comparison of these two snowflakes reveals markedly different temporal firing patterns under the two behavioral conditions. In the first condition, the neuron tended to fire in burst of three spikes in response to the tone stimulus (Fig. 5A). This tendency, however, was strongly decreased when the same tone stimulus was associated with the opposite motor response, as expressed

by the lack of dark bins around the center in Fig. 5B. Note also that, while the firing patterns of the neuron clearly differ in the two cases, the firing rate is not very different (0.73 spikes/sec as compared to 0.99 spikes/sec).

Conclusion

The above discussion of single-neuron firing codes was by no means intended to be exhaustive. Several other single-neuron neural coding schemes have been pursued, with varying degrees of success. For an early overview of potential single-neuron codes we refer to the classical work of Perkel and Bullock (1968). As a more recent example we mention the work of Richmond and Optican, who proposed a rate code in the visual cortex, which explicitly takes into account the full time course of the firing rate profile (e.g. Richmond and Optican 1987; Optican and Richmond 1987).

Summarizing the findings on single-unit activity in the cortex, both in terms of firing rates and firing patterns, we conclude that:

1. Usually, single-neuron activity consists of a transient response, followed by a long lasting epoch of increased firing rate. The activity may be related to external events, such as sensory stimuli or specific movements, but also to other aspects of behavior, such as intentions to make movements or sensorimotor associations. A single cortical neuron may be active for hundreds of milliseconds to several seconds after the stimulus has disappeared, so that 'something must keep it going'.
2. Higher order neurons show selectivity in a manner which can only be explained by convergence from simple to more complex features. This convergence can be envisaged in at least two different ways, one leading to highly specific grandmother neurons, the other to neurons that can participate in more than one functional group (assembly?). The existence of two independent components of activity as in Fig. 2 suggests that a single neuron may participate in more than one process.
3. If neurons are involved in computation and coding only when their firing rates are elevated, it turns out that most cortical neurons are idle for most of the time. Searching for alternative coding schemes, it could be shown that the temporal firing pattern of single cortical neurons may also serve as a potential neural code.

Cortical activity at the level of multiple-neuron spike trains

In spite of the success in the search for codes in cortical single-neuron activity, there is obviously room for alternative proposals. Clearly, the brain is more than just a collection of single neurons, each living in 'splendid isolation'. They also exert influences onto each other through their anatomical connections. Just as in physics the 'ideal gas' theory of non-interacting particles was considered a first and quite adequate approximation, later approaches emphasized the importance of incorporating the interactions among these particles. Similarly, researchers for a long time have looked for codes which reside in the activity of ensembles of neurons.

One of the first to formulate this approach was Hebb (1949). He suggested that the coherent activity within functional groups of neurons ('cell-assemblies'), mediated by anatomical, presumably plastic connections, forms the basis of the neural code. The groups, he hypothesized, are formed by modifications of synaptic strength that obey what later became known as Hebb's rule: "When an axon of cell A is near enough to excite a cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place such that A's efficacy, as one of the cells firing B, is increased." (Hebb 1949).

Hebb's hypothesis concerning the functional role of cell assemblies in central processing was adopted widely among theoretically inclined researchers. In fact, it lay the conceptual foundation for most of the current work on 'neural network theories' of brain function (e.g. Braitenberg 1978; Edelman 1981; Abeles 1982a; Palm 1982; Hopfield 1982; Hopfield and Tank 1986; Palm and Aertsen 1986; Rumelhart et al. 1986; Amit 1989). However, there are very little experimental data that challenge the cell assemblies hypothesis. Almost all the above models assume that 'learning' is based on selective modifications of the connectivity among neurons, and that 'computations' are carried out by selective activation of groups of interconnected neurons. According to these hypotheses, the neural code resides in correlated activity within and between neuronal groups. Hence, neither the study of the overall activity in large populations of neurons, nor the recording of single-neuron activity, one at a time, allow for a critical test of the assembly concept. In order to gain an understanding of the processes taking place within and between hypothetical neuronal assemblies, the ex-

perimental methodology must involve simultaneous recording of many neurons in parallel, preferably in awake, behaving animals. This enables one to observe simultaneously and separably the activities of many neurons, while they are participating in meaningful processing and computational tasks, and to analyze these activities for possible signs of (dynamic) interactions (Gerstein et al. 1989). Indeed, recent years have shown a growing interest in the simultaneous recording and analysis of spike trains from groups of up to some 10-30 neurons (Abeles 1982a, 1991; Gerstein et al. 1983; Krüger 1983; Eggermont 1990). Associated with this, new computational tools were developed to analyze and interpret the large flow of information coming from such 'multi-neuron' experiments.

Ideally, one should study the activity in a cell assembly by recording the activity of all the neurons in the region in which the cell assembly resides. With the current technology of 'spike sorting' devices, one can hope to record spike activity of a few single neurons (up to six) through one microelectrode (e.g. Abeles and Goldstein 1977) and up to 30 neurons by using multiple electrodes (Krüger 1983; Gerstein et al. 1983). At best, therefore, we can tap only a few members of a hypothetical neuronal network. Nevertheless, it is appropriate to examine how the available physiological data support different concepts and models of neural codes, in quest of an optimal research strategy.

Multiple-neuron firing as a neural code

Several attempts have been made to extend the notion of single-neuron firing rate as a coding mechanism to the activity exhibited by ensembles of neurons. The most notable examples of this approach of *multi-neuron firing rates* as a code can be found in the study of the motor cortex (e.g. Georgopoulos et al. 1988, 1989) and the coding of saccadic eye movements (e.g. van Gisbergen et al. 1987; Lee et al. 1988). Briefly, the firing rates of the various members of the ensemble, usually all neurons in an activated patch of neural tissue, are combined into a 'population vector', which ultimately specifies the direction of the movement to be made. Each single neuron contributes an elementary component to this population vector, the direction of which is determined by the neuron's specificity in terms of the associated movement, and its magnitude by the neuron's firing rate. Related approaches have been proposed for the visual cortex, with the popula-

tion vector being defined either in the external, visual space (e.g. Vogels 1990) or in an internal, neural activity space (see the contribution of Gerstein and Gochin in this Volume).

Also the *firing patterns* in multi-neuron activity have been invoked in several population coding schemes. An early attempt is found in the concept of 'multi-unit receptive field', introduced by Stevens and Gerstein (1976). A vector-type approach, with the population vector defined in sensory space but based on the instants of multi-unit spike firings rather than their rates, was proposed for the auditory system by Johannesma (1981; see also Gielen et al. 1988; Hesselmans and Johannesma 1989); similar ideas were later applied in the visual system (Bialek et al. 1991). A transition between a rate and a pattern code was proposed for the visual cortex by Krüger (1991; see also Krüger and Becker in this Volume); similarly to Gerstein's proposal, his population vector is defined in neural activity space.

Alternative pattern codes, which do not resort to the notion of a population vector, but instead look at the detailed temporal pattern of multi-unit firing were investigated by Legendy and Salcmann (1985) and Frostig et al. (1985). Pattern codes, based on the notion of 'synfire chains' (Abeles 1982a) were studied by Abeles and Gerstein (1988; see also Abeles 1991). More recently, and inspired by recent findings on oscillatory firing behavior in the cat visual cortex (Gray and Singer 1989; Gray et al. 1989; Eckhorn et al. 1988 and in this Volume), several models have been proposed which invoke the notion of 'dynamic linking' (von der Malsburg 1981, 1986) as a mechanism by which multi-neuron activity reflects information about the visual world. In most of these models, the linking of neurons into functional groups is mediated by the synchronization of oscillatory activity (e.g. Sporns et al. 1989; Sompolinsky et al. 1990, 1991; König and Schillen 1991; Schillen and König 1991; Eckhorn et al. 1990, 1991). An alternative model, which emphasizes synchronization rather than oscillation as the principal information carrying device was proposed by Neven and Aertsen (1992; see also Johannesma et al. 1986; and Erb and Aertsen in this Volume).

Response properties of neighboring cortical neurons

Many of the above mentioned multi-unit coding schemes rely essentially on the idea of 'functional maps'. Briefly, this concept is used to

describe findings that the functional properties of neurons are distributed over the cortical surface in a topologically ordered way. In particular, it is also used to indicate that neurons at anatomically neighboring positions have 'neighboring' functional properties. The most notable examples of functional maps in the cortex are the columnar systems proposed for the somatosensory cortex (Mountcastle 1957, 1977) and the visual cortex (Hubel and Wiesel 1968, 1977; see also the contributions of Bonhoeffer and Grinvald, Löwel and Braitenberg in this Volume). In order to investigate to what extent this concept holds as a general organizational principle for cortical representations, we examined in two sets of experiments the relations between the firing behaviors of neighboring neurons in the primary auditory cortex and in the granular frontal 'association' areas (Vaadia et al. 1991). Typical examples of our findings are given in Figures 6 and 7, which show the activity of two sets of adjacent neurons recorded simultaneously in each of these two cortical fields.

Figure 6 shows the multi-neuron activity, recorded by five microelectrodes arranged in a circle, from the primary auditory cortex of an alert Rhesus monkey. Three electrodes recorded more than one isolated neuron each (units 2 and 3; units 4 and 5; and units 7, 8 and 9). Each of the nine raster-display bands depicts a single neuron's activity, recorded over a number of trials of 1.2 seconds each. Individual traces are locked in time to the onset of a stimulus (at time=0), which consisted of 3.4 kHz tone bursts of 300 msec duration at an intensity of 68 dB SPL. This result clearly demonstrates that a number of neurons within the recording area shared certain functional properties and responded to the same stimulus (neurons 1, 4, 5, 6 and 7). However, it is also evident that the response patterns of some of these neighboring neurons differed, and that some of them did not respond at all to the stimulus. For example, while units 1 and 5 responded very strongly to the tone stimuli, the activity of units 2 and 8 was virtually unaffected. Notice also that this strong variability of firing behavior was seen even among neurons that were recorded by the same electrode (for example, units 7, 8 and 9). The distance separating these neurons is probably less than 100 μm (Abeles et al. 1975). The dogma of columnar organization of the auditory cortex implies that all the neurons in the same column share the same best frequency. Although the results shown in Fig. 6 are consistent with this dogma, they evidently do not support the simplistic interpretation that the neurons within a column are all activated in unison.

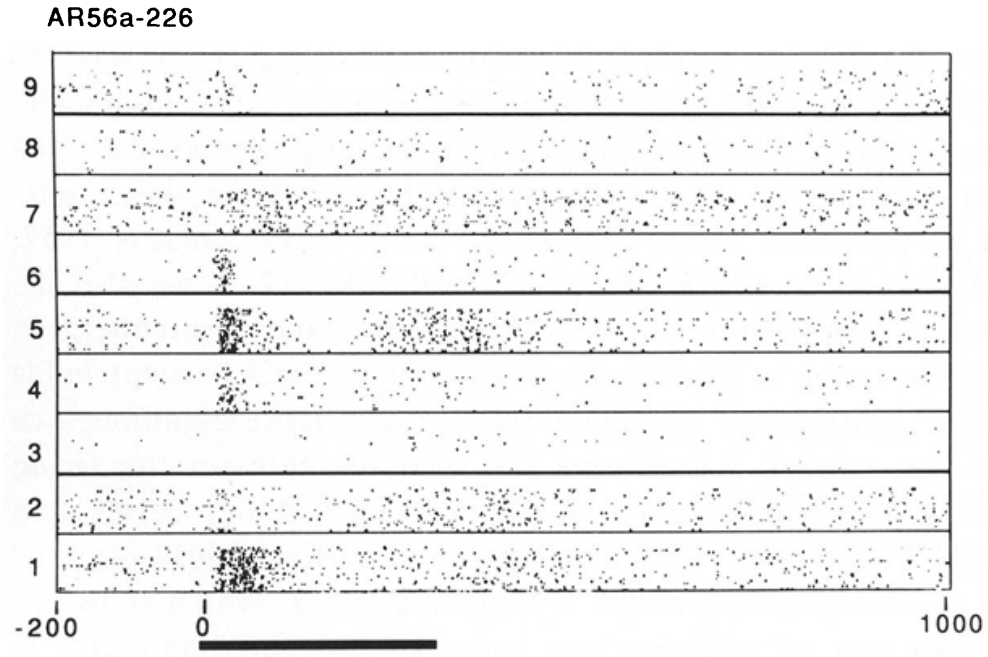


Fig. 6. Raster displays of the responses to tone bursts of 9 neurons in the primary auditory cortex of the Rhesus monkey. The stimulus (a tone burst of 3.4 kHz at 68 dB SPL) is marked by a black bar under the abscissa. The neurons were recorded by 5 microelectrodes. The first electrode recorded unit 1; the second: units 2 and 3; the third: units 4 and 5; the fourth: unit 6; and the fifth: units 7, 8 and 9. Note that neurons 1, 4, 5, 6 and 7 respond to the stimulus, whereas some of the neighboring neurons, e.g. 2 and 8, do not respond at all. This strong variability of firing behavior was seen even among neurons that were recorded by the same electrode (for example, units 7, 8 and 9) (From Vaadia et al. 1991)

The study of neuronal activity in the 'non-specific' association areas poses some difficulties. The functional organization is not very well known and the majority of neurons do not respond at all to sensory stimuli. It is important to study these areas, however, if we wish to examine the mechanisms involved in higher brain functions. To examine the properties of adjacent neurons related to higher functions, one should carefully select and match a recording area with an appropriate, controlled behavioral task. Previous studies in primates have demonstrated that the projections to the prefrontal cortex are segregated in the form of vertical columns (Goldman and Nauta 1977; Goldman-Rakic 1987), and that areas within the frontal cortex are related to higher brain functions (Butters and Pandya 1969; Passingham 1975; Niki and Watanabe 1976, 1979; Evarts et al. 1984; Petrides 1986; Watanabe 1986a,b; Goldman-Rakic 1987; Fuster 1989, and many

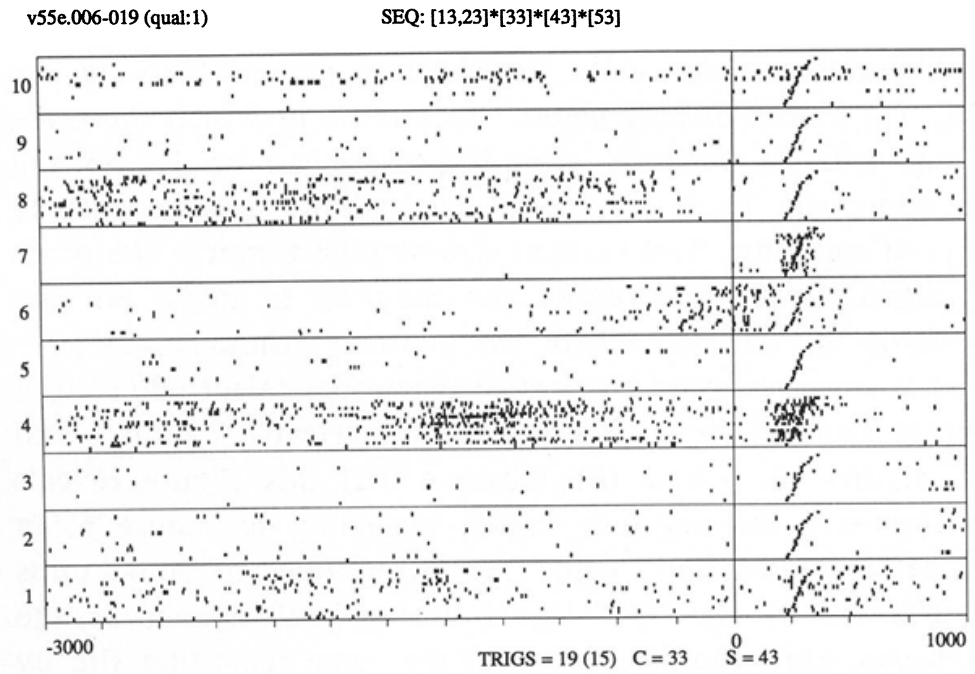


Fig. 7. Raster displays of the activity of 10 neurons in the frontal cortex of a monkey during performance of a localizing task. The rasters show 4 seconds of activity centered around the onset-time of the GO-signal. The trials are sorted (from bottom to top of each strip) according to the reaction time (the time from the onset of the GO-signal to the initiation of arm movement (marked by small crosses). The activity was collected from correct trials where the auditory spatial cues were presented in the left (contralateral) hemifield, at 15° from the midline. The units were recorded by 5 microelectrodes. The first electrode recorded unit 1; the second: units 2 and 3; the third: units 4 and 5; the fourth: units 6 and 7; and the fifth: units 8, 9 and 10. Note the task-related activity of the units 1,4,6,7, while the neighboring units (2,3,5,9) were practically unaffected by behavioral events. (From Vaadia et al. 1989)

others). It was also found that many neurons in the vicinity of the arcuate sulcus responded to both auditory and visual stimuli, when the stimulus served to cue the direction of movements (Vaadia et al. 1986). The combined results of some of the above studies suggest that neuronal activities related to sensory analysis, sensorimotor association, and preparation or execution of movements may be found in the same area. Thus, the frontal cortex seems to be a good place to study neuronal interactions in behaving animals.

In order to study the activity of neighboring neurons in this area, monkeys were trained to perform a spatial task with delay, in which the monkey had to localize auditory and visual stimuli (for details see Vaadia et al. 1991). Figure 7 presents an illustrative example of the

neuronal activity in a group of ten neurons in the frontal cortex, that were recorded simultaneously while the monkey was performing the localizing task. The raster-display shows those trials in which the relevant spatial cue was an auditory stimulus, presented at 15° in the contra-lateral hemifield. Each of the 10 strips shows a raster display for the activity of one unit. The vertical line at time 0 marks the onset of the 'GO' signal, which instructed the monkey to make an arm movement towards the location where the auditory stimulus was presented. The units were recorded by 5 microelectrodes (electrode 1: unit 1, electr. 2: units 2 and 3, electr. 3: units 4 and 5, electr. 4: units 6 and 7, and electr. 5: units 8, 9 and 10). Observe that this Figure reveals many similarities with the auditory cortex recording in Figure 6. In particular, it demonstrates that, while the firing rates of some units were clearly affected by the 'GO'-signal during performance of the task, other neurons, even those recorded at the same recording site by the same microelectrode, were not affected at all.

Conclusion

The pattern revealed in Figures 6 and 7 was found to repeat at many other recording sites. Neighboring units could be activated under similar conditions, but could also have different response properties. Moreover, responsive neurons were intermingled with non-responsive neurons. Summarizing, we conclude that:

Neighboring neurons may be functionally related and share common features. However, even when neurons were recorded by the same microelectrode, they were not all activated in unison. These findings suggest that the functional organization of each small volume of cortex allows for the co-existence of functionally distinct neurons, which may participate in several different processes.

Interactions between neighboring cortical neurons

In order to assess the extent to which neurons with similar response properties organize into functional groups, we analyzed the interactions taking place between these neurons. The analysis of interactions among

neurons usually consists of cross-correlating spikes from pairs (sometimes triplets) of neurons and inspecting the results for possible signs of 'functional' or 'effective' connectivity (Moore et al. 1966; Perkel et al. 1967, 1975). Recent developments have expanded the scope of these studies. Methods were developed in an effort to reveal global cooperativity in groups of neurons (Gerstein et al. 1985; Gerstein and Aertsen 1985; Aertsen et al. 1986, 1987) and to study in detail the dynamic properties of the correlation between two neurons (Gerstein 1988; Aertsen et al. 1989).

Figure 8 illustrates different types of cross-correlograms obtained from pairs of neurons in the auditory cortex and the frontal cortex of awake monkeys during 'non-performance' periods, i.e. when no stimuli were delivered and the monkey did not perform the task. Fig. 8A shows an example of *uncorrelated* activity: the firing probability of the first cell did not change significantly before or after the firing of the other. About 30% of the neuron pairs recorded from the same microelectrode showed such uncorrelated activity (Vaadia et al. 1991). In some cases a narrow peak confined to one side of the origin could be observed (Fig. 8B). The interpretation that these correlograms reflect a *direct excitatory connection* between the two neurons is supported by the finding that most of these one-sided peaks were found among neurons that were recorded by the same microelectrode, but never among neurons that were more than 600 μm apart. Signs of a *direct inhibitory connection* (a one-sided trough) were found in only very few cases. This is not surprising, however, in view of the low sensitivity of cross-correlation for inhibition under conditions of low firing rates (Aertsen and Gerstein 1985), as typically found in this part of the cortex (Abeles et al. 1990). In the sample of neuron pairs that were recorded by one microelectrode, signs of such 'direct connections' (excitatory and inhibitory) were found in about 20% of the cases, most of them weaker than the example in Fig. 8B (Vaadia et al. 1991).

By far the most common type of interaction found (30% of all pairs; Vaadia et al. 1991) was a more or less symmetrical peak straddling the origin. This type of interaction came in two variants, distinguished by the width of the two-sided peak: *wide* (more than 200 ms; Fig. 8C) and *narrow* (15-100 ms; Figs. 8D,E). Cross-correlograms of this type could emerge when the two neurons shared common excitatory or inhibitory inputs. Two-sided peaks could also emerge when the two neurons excited each other (although this interpretation is highly unlikely for the wider peaks). In most cases the peak gradually

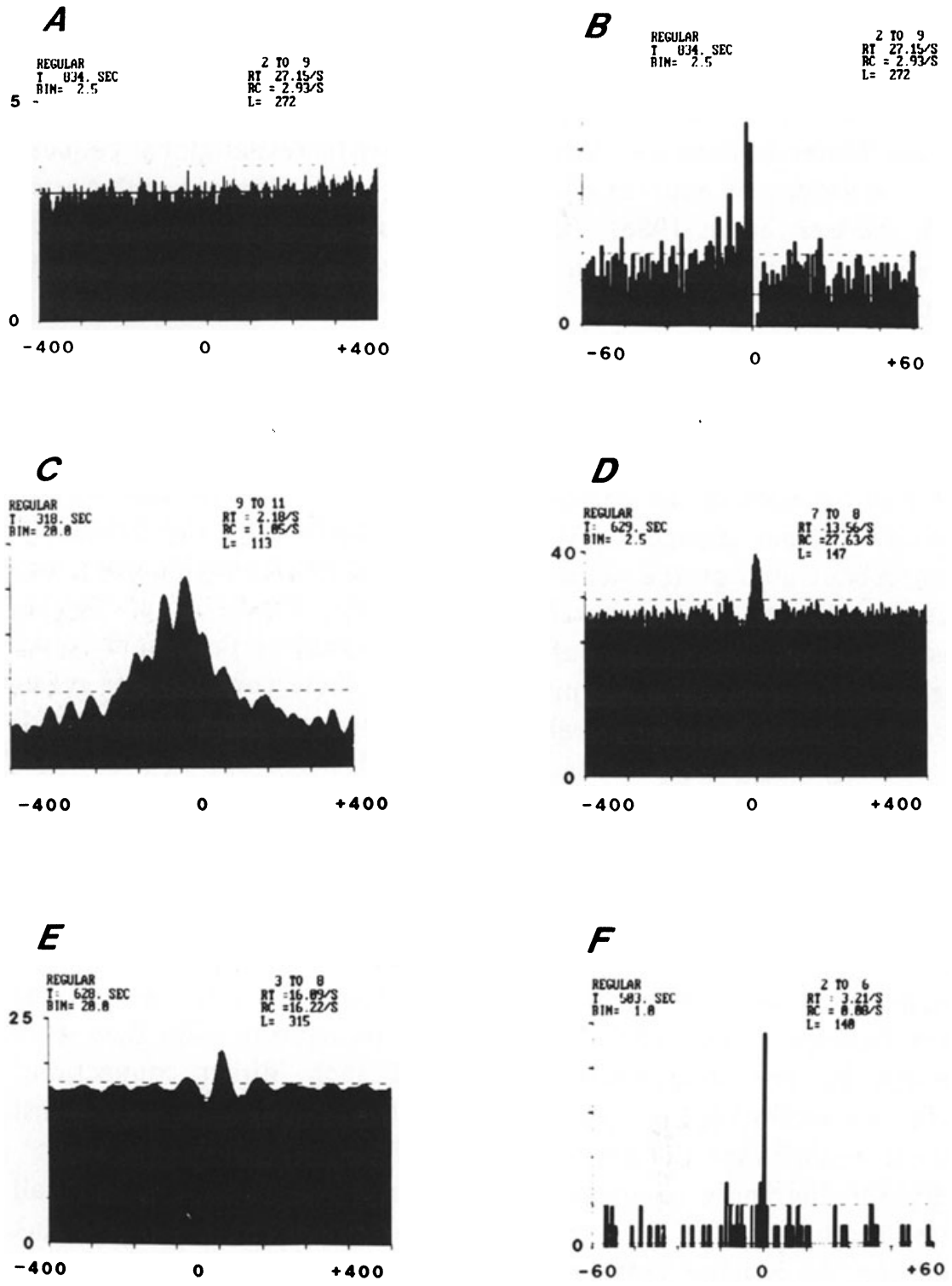


Fig. 8. Cross-correlograms between pairs of neurons in the auditory cortex and the frontal cortex of awake monkeys during 'non-performance' conditions. The abscissa describes the time (ms) around the firing of one neuron, the ordinate describes the firing rate (spikes/s) of the other neuron. The labels on each correlogram give the total data collection time (T), the average firing rate of the two neurons (RT and RC), the bin size (BIN), and the number of data sections (L). For each correlation,

decayed with increasing time interval to the reference spike. In a few cases, there were weak signs of periodicity in the cross-correlograms, as demonstrated in Fig. 8E. The periodicity was in all cases at a frequency of less than 14 Hz. Interestingly, the probability of finding 'narrow' two-sided peaks decreased rapidly with the distance between the cells: according to a preliminary investigation (Lavner 1989) such interaction was found among 30-40% of the pairs recorded by the same microelectrode, as opposed to only 3-8% of the pairs that were 500-600 μm apart. In contrast to this, the probability of finding 'wide' two-sided peaks did not show a clear dependence on pair distance for distances up to 1 mm; within that range the overall frequency of occurrence was 10-20%. Finally, several previous studies reported 'ultra-narrow' peaks of 1 msec or less in cross-correlograms (Toyama et al. 1981; Allum et al. 1982; Murphy et al. 1985; Lurito et al. 1988). An example of such an 'ultra-narrow' peak is shown in Fig. 8F. This correlogram indicates that some spikes of the two units were highly synchronized. This type of cross-correlogram was very infrequent in our studies. A possible explanation may lie in the technological difficulty of detecting two spikes that occur at the same time using a single electrode.

The *width* of the two-sided peak reflects the degree of synchronization of the two neurons and, hence, the time-scale of the processes that affect them. Whether 'narrow' and 'wide' peaks reflect different type of interactions is an still open question. Nevertheless, it is reasonable to hypothesize that the narrow peaks reflect local direct co-activation of relatively small groups of neurons, while the wide peaks reflect a more general co-activation of larger groups of neurons in a relatively wide-spread cortical area. Ultra-narrow peaks were sometimes found at time delays different from zero, which suggests that groups of neurons can fire in precise synchrony and transmit information with high temporal accuracy.

The *area* under the two-sided peak was on the average 0.06 spikes. This area, which equals the correlation coefficient, indicates to what extent the two neurons tend to discharge in synchrony. The low values

---

a band of 99% confidence limits for the equivalent, independent Poisson processes (Abeles 1982b) is shown by broken lines. A: Uncorrelated activity. B: 'One-sided' narrow peak. (Note the time scale: 60 ms) C: 'Two-sided' wide peak. D: 'Two-sided' narrow peak. E: 'Two-sided' peak with slight signs of periodicity. F: 'Ultra-narrow' peak at time 0 (time scale: 60 ms). (From Vaadia et al. 1991)

that we usually measured suggest that most impulse discharges were not correlated. That is, most of the spikes fired by two neurons that shared a common excitatory input originated from EPSPs of other excitatory inputs, which drove each of the neurons independently. This finding confirms the results of previous studies, where triple cross-correlograms (compare the 'snowflakes' in Fig. 5) were used to demonstrate that a single neuron may share common-input with an adjacent neuron from one source, while another input drives the same neuron in unison with another neuron (Abeles 1983; Abeles et al. 1983; Frostig et al. 1983; Vaadia and Abeles 1987).

Conclusion

From these and many similar findings we conclude that:

1. The interactions among adjacent neurons as revealed by cross-correlation analysis are mostly of the 'two-sided', less often of the 'one-sided' type.
2. Usually the observed interactions between neuron pairs are weak, in the sense that many of their spikes are not correlated, even among neurons that have similar functional properties.
3. It is likely that the neurons receive some correlated inputs and other independent inputs. We speculate that the three types of 'two-sided' peak width in cross-correlograms reflect three different mechanisms of neuronal interactions. The 'ultra-narrow' peaks reflect the activity in 'synfire chains', the 'narrow' peaks reflect local co-activation of neurons, and the 'wide' peaks reflect a more general asynchronous mechanism affecting large cortical areas.
4. Oscillating interactions (40-70 Hz) have been reported between cells in the cat visual cortex, that respond with oscillatory firing to adequate visual stimuli. Although oscillatory single-neuron firing in that frequency range was also observed in the somatosensory cortex, not a single case of oscillatory interaction was found there. Oscillations in that frequency range are conspicuously absent in the auditory cortex and the frontal cortex, both in single-neuron firing and in neuronal interactions.

Modifications of neuronal interactions

Modifications in relation to sensory or behavioral events

One of the consequences of Hebb's cell assembly hypothesis would be that neurons organize into functional groups, depending on the momentary computational demand. This would imply that the interactions among neurons should be variable, in particular that they should be modified in relation to behavioral state, or to the presentation of relevant sensory stimuli. Such dependencies on sensory stimulation, arousal levels and behavioral state have indeed been observed (e.g. Dickson and Gerstein 1974; Gassanov et al. 1980; Abeles et al. 1983; Eggermont et al. 1983; Frostig et al. 1983; Eckhorn et al. 1988; Gray and Singer 1989; Aertsen et al. 1987; Krüger and Aiple 1988; Aertsen and Gerstein 1991; Vaadia et al. 1991). We present here two illustrative examples of such modification of interactions by behavioral and stimulus events, one from the auditory cortex, the other from the prefrontal cortex.

Figure 9 shows an example where the spike correlation between two cortical neurons was influenced by a sensory stimulus (from Ahissar et al. 1992). The Figure illustrates the different interactions between two neurons in the auditory cortex of a monkey during presentations of two sound movements in opposite directions. A statistically significant peak can be seen in the first cross-correlogram, computed for the intervals when the stimulus was moving from right to left (Fig. 9A). The position of the peak indicates that the probability of detecting a spike of neuron 9 was increased for about 30 msec after neuron 3 fired a spike. However, when the sound stimulus was moving in the opposite direction (from left to right; Fig. 9B), the interaction between the same two neurons was distinctly different. The correlation in this case was very weak and seems to reflect an opposite interaction, namely, a weak direct inhibitory connection, again from neuron 3 onto neuron 9. Note that the PST histograms of these neurons do not show any such sensitivity; both of them responded with a very similar on-response to the two stimuli (Figs. 9C to 9F). Joint-PST analysis (see next Section) for these two neurons showed that both the peak (Fig. 9A) and trough (Fig. 9B) in the corresponding cross-correlograms originated from spikes fired during the on-response of the two neurons; no significant correlation was observed during the remainder of the response.

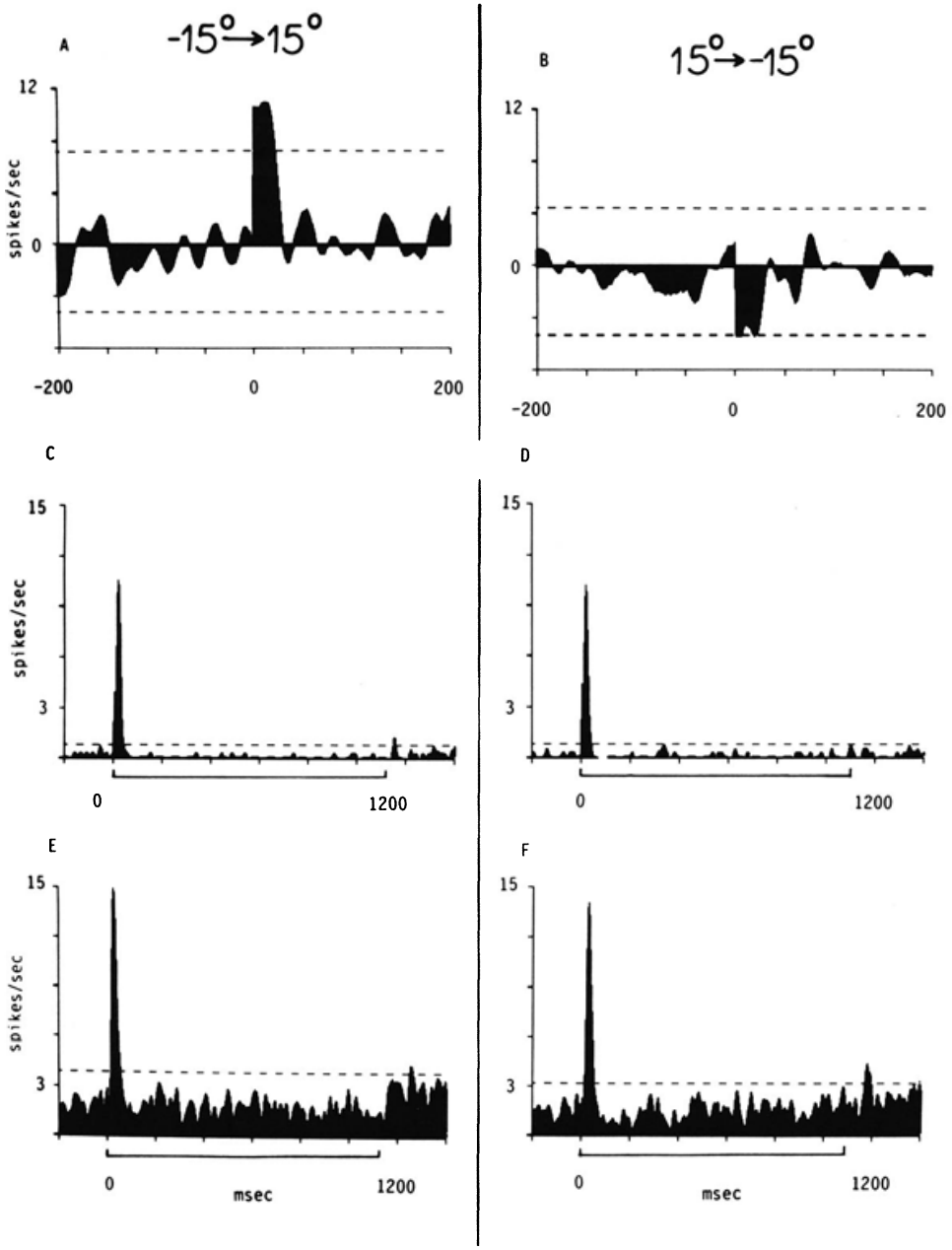


Fig. 9. Modification of interactions in the auditory cortex by sensory stimuli. Example of direction sensitivity, expressed only in the interaction between two neurons, and not in any one of the two single-neuron response profiles. **A-B**: Difference-correlograms of units 3 and 9, computed from data segments recorded during presentation of moving stimuli: A) rightwards (-15° to +15°); B) leftwards (+15° to -15°). **C-F**: PST-histograms showing the responses of units 3 (C,D) and 9 (E,F) to the two stimuli moving in opposite directions (N=291 stimuli for rightward movements; N=295 stimuli for leftward movements). Correlograms and PST-histograms were smoothed, using a gaussian with sigma=15 ms. (From Ahissar et al. 1992)

An example of an interaction that was modified in relation to behavior is presented in Figure 10. It shows the correlation between the

spike trains of two prefrontal cortex neurons, collected from two different time sections while the monkey was engaged in the delayed-localization task (cf. Fig. 7). The spike trains in Fig. 10A were recorded during intervals of 1 second, during and immediately following the presentation of a visual stimulus at 30° on the left. The data in Fig. 10B were collected from sections of inter-trial intervals (ITI; 3 seconds each). Comparison of these two correlograms shows that there is a marked difference in the interactions during the two behavioral conditions. An irregular, but very distinct, two-sided peak of the narrow type can be observed when the monkey was presented with the visual stimulus, while the spike trains recorded during the inter-trial intervals show no correlation at all. We note that in the actual trials, these two conditions were separated in time by at most a few seconds.

Dynamical properties of neuronal interactions

It is quite conceivable that these changes of interaction induced by sensory and behavioral events are due to rapid modulations of discharge synchronization among the neurons. Unfortunately, the ordinary cross-correlogram, representing a time-averaged count of near-coincident spikes, does not allow to examine the time course of such possible changes. Recent developments in analysis methodology, however, have overcome this problem. In particular, the *Joint-PSTH* (Aertsen et al. 1989; Palm et al. 1988) was designed to highlight the detailed time structure of firing correlation among two neurons, and its possible time-locking to a third event, such as a stimulus or behavioral event. Moreover, appropriate normalization of the Joint-PSTH enables us to distinguish between contributions due to stimulus- or behavior-induced modulations of the single-neuron firing rates, and those from interneuronal correlation, the latter reflecting the *'effective'* or *'functional connectivity'* among the neurons involved.

Figure 11 shows an example of the results of such Joint-PSTH analysis and the dynamic changes of pair interaction revealed by it. Data were collected from two different time sections of spike trains from two frontal cortex neurons during performance of the same localization task as used in Figure 7. The first section comprises 600 ms immediately following the GO-signal (Fig. 11A), the second one covers an interval of 600 ms, starting 900 ms after the monkey's hand left the target key (after it hit the correct location, and the monkey

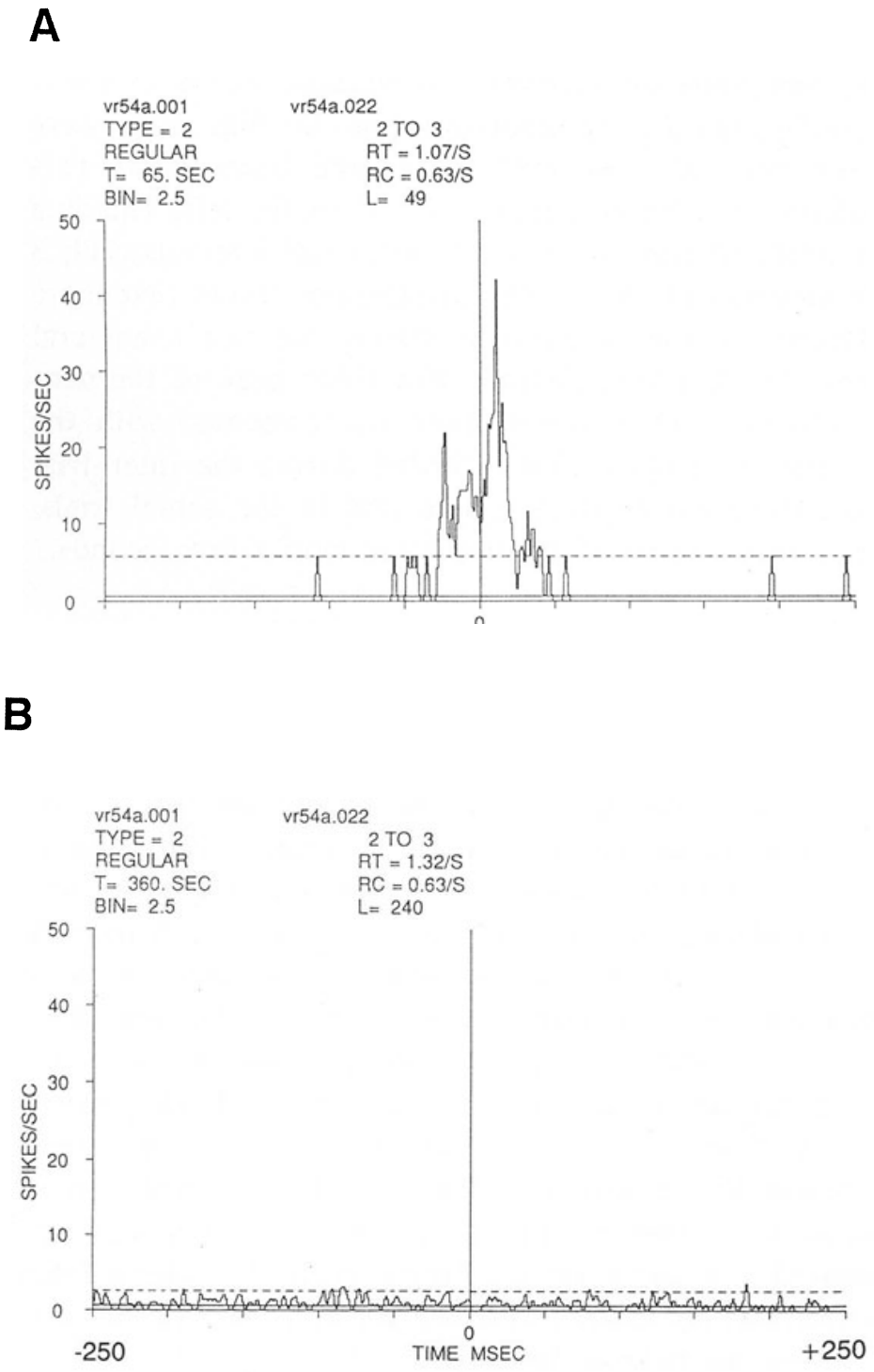
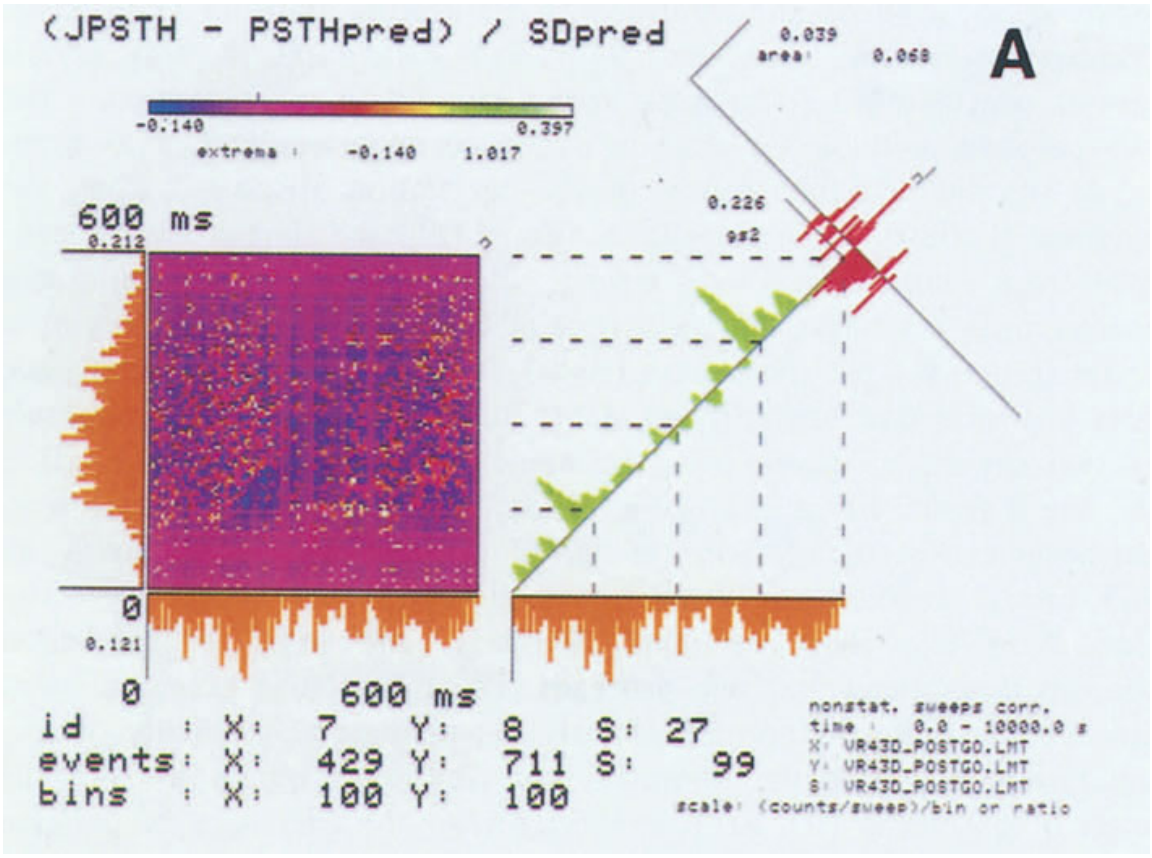
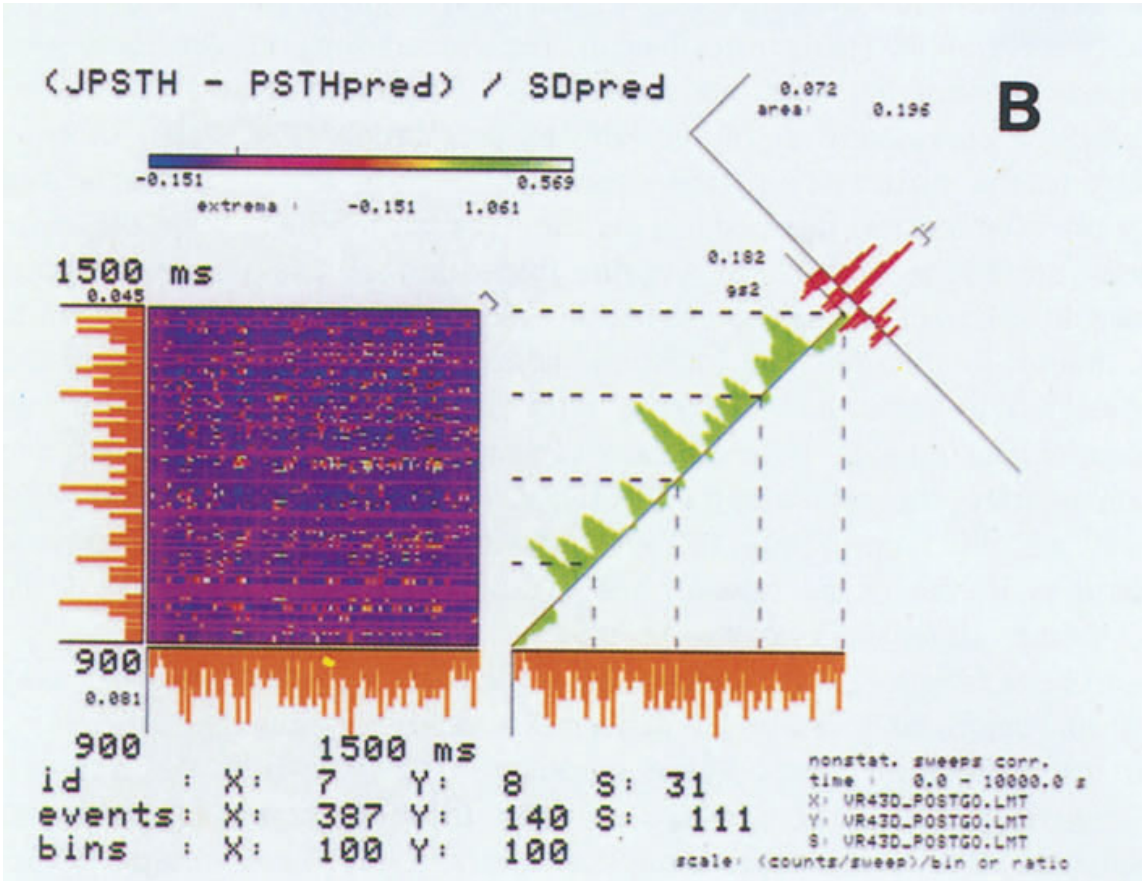


Fig. 10. Modification of interactions in relation to behavioral state. Two cross-correlograms of one pair of neurons recorded in the prefrontal cortex of the monkey during performance of the delayed localization task. The cross-correlogram in **A** was computed from sections of activity, recorded during intervals of 1 second, during and immediately following the presentation of a visual stimulus at 30° on the left. The cross-correlogram in **B** was computed from sections of inter-trial intervals (ITI; 3 seconds each). Observe the marked difference in the interactions during the two behavioral conditions. Note that in the actual trials, these two conditions were separated in time by at most a few seconds.

received its reward) and returned to its resting position (Fig. 11B). Comparison of the normalized Joint-PST histograms in both panels reveals considerable differences in the interaction patterns among the two neurons, both in the time-averaged correlograms and, even more so, in the detailed time course of the correlation, displayed along the diagonal. Following the GO-signal (Fig. 11A), the time-averaged correlation is characterized by a strong, 'bi-phasic' interaction pattern: a narrow peak for negative delays (left of the origin), accompanied by a wider trough for positive delays (right). Interestingly, the positive peak does not reflect an ongoing and stable interaction, but is the net result of two extremely short-lasting instances of discharge synchronization (cf. the diagonal histogram in Fig. 11A), occurring in coincidence with the onset and offset of firing of one of the two neurons (compare the PST-histogram along the y-axis), with no interaction whatsoever outside these two short intervals. Similarly, the negative interaction changes dramatically as time proceeds. The time tourse of modulation, however, is quite different: a sharply increasing and gradually decaying negativity, with the dominant contribution originating from the onset phase of the first neuron, shortly after the first peak of positive interaction, when also the second neuron (PST-histogram along the x-axis) elevates its firing rate. During the second time section, however, separated from the first one by a mere 1.5 s, these same two neurons exhibit a completely different type of correlation (Fig. 11B). In contrast to the earlier result, the overall interaction now is characterized by an asymmetric, damped-oscillation-type correlation, with the main peak straddling the origin. Again, inspection of the diagonal region reveals distinct signs of dynamic modulation of the interaction. Although in this case the increased noise level (presumably due to the considerable reduction in firing rates of both neurons) prohibits an unequivocal parsing into separate components, there are hints of two non-overlapping oscillatory subpatterns (extending roughly from 900-1100 ms and from 1200-1400 ms), possibly associated with concurrent features in the firing rate of one of the neurons (compare the PST-histogram along the x-axis).

This example clearly demonstrates that the neurons' activities may exhibit rapid modulations of discharge synchronization that are related to the behavioral state. These modulations may switch the neurons' firing behaviour from being mutually incoherent into a particular coherent state of joint synchrony, or, alternatively, from one particular pattern of mutual coherence into a different one. Each such pattern


(JPSTH - PSTHpred) / SDpred
A
-0.140
0.397
extrema : -0.140 1.017
600 ms
0.212
0
0.121
0
600 ms
0.039
area: 0.068
0.226
gs2
id : X: 7 Y: 8 S: 27
events: X: 429 Y: 711 S: 99
bins : X: 100 Y: 100
nonstat. sweeps corr.
time : 0.0 - 10000.0 s
X: VR43D_POSTGO.LMT
Y: VR43D_POSTGO.LMT
S: VR43D_POSTGO.LMT
scale: (counts/sweep)/bin or ratio


(JPSTH - PSTHpred) / SDpred
B
-0.151
0.569
extrema : -0.151 1.061
1500 ms
0.045
900
0.081
900
1500 ms
0.072
area: 0.196
0.182
gs2
id : X: 7 Y: 8 S: 31
events: X: 387 Y: 140 S: 111
bins : X: 100 Y: 100
nonstat. sweeps corr.
time : 0.0 - 10000.0 s
X: VR43D_POSTGO.LMT
Y: VR43D_POSTGO.LMT
S: VR43D_POSTGO.LMT
scale: (counts/sweep)/bin or ratio

may last for only a few tens to hundreds of milliseconds. Finally, the observed modulations in synchronized firing may be, but are not necessarily associated with changes in either of the neurons' individual firing rates.

Interactions among larger groups of neurons

So far we only addressed the issue of correlation between two neurons at a time. An important question in view of the hypothesis that neurons dynamically organise into functional groups, is whether correlations also exist between larger groups of neurons, and, if so, whether such group correlations follow a similar pattern as the pair correlations do, particularly regarding their dependence on behavioral state. In order to study the global firing correlations among entire groups of simultaneously recorded neurons, we used the *gravitational clustering* analysis (Gerstein et al. 1985; Gerstein and Aertsen 1985; Aertsen et al. 1986, 1987; Aertsen and Gerstein 1991). This conceptual framework and analysis technique was explicitly designed to deal with population activity, in particular for the detection of co-activation of larger numbers of neurons. We give here only a brief description and refer to the original literature for more details.

Fig. 11. Dynamics of neuronal interaction. Joint-PSTH analysis of two simultaneously recorded neurons from the frontal cortex of a monkey during performance of the 'delayed localization' task. The color-coded, normalized Joint-PSTH matrices in both panels represent the time-dependent correlation of firing among the two neurons, after normalization for stimulus-induced modulations in single-neuron firing rates. The latter are assessed by the PST-histograms shown along the horizontal and vertical axes. The diagonal band of the normalized Joint-PSTH matrix reflects the near-coincident firing correlation as it evolves in the course of time; it is shown once again in the diagonal histogram in the right-hand part of the Figures (lower left to upper right). Finally, the normalized cross-correlogram is obtained by integrating along the diagonal; it is shown in the second histogram in the right-hand part of the Figures (upper left to lower right). Data was collected from two different time sections of spike trains: **A**: Time section of 600 ms immediately following the GO-signal; **B**: Interval of 600 ms, starting 900 ms after the monkey's hand left the target key (after hitting the correct location, and the monkey received its reward) and returned to its resting position. Notice the clear differences in correlation during these two time sections, separated from each other by only about 1.5 s. Further explanation in text.

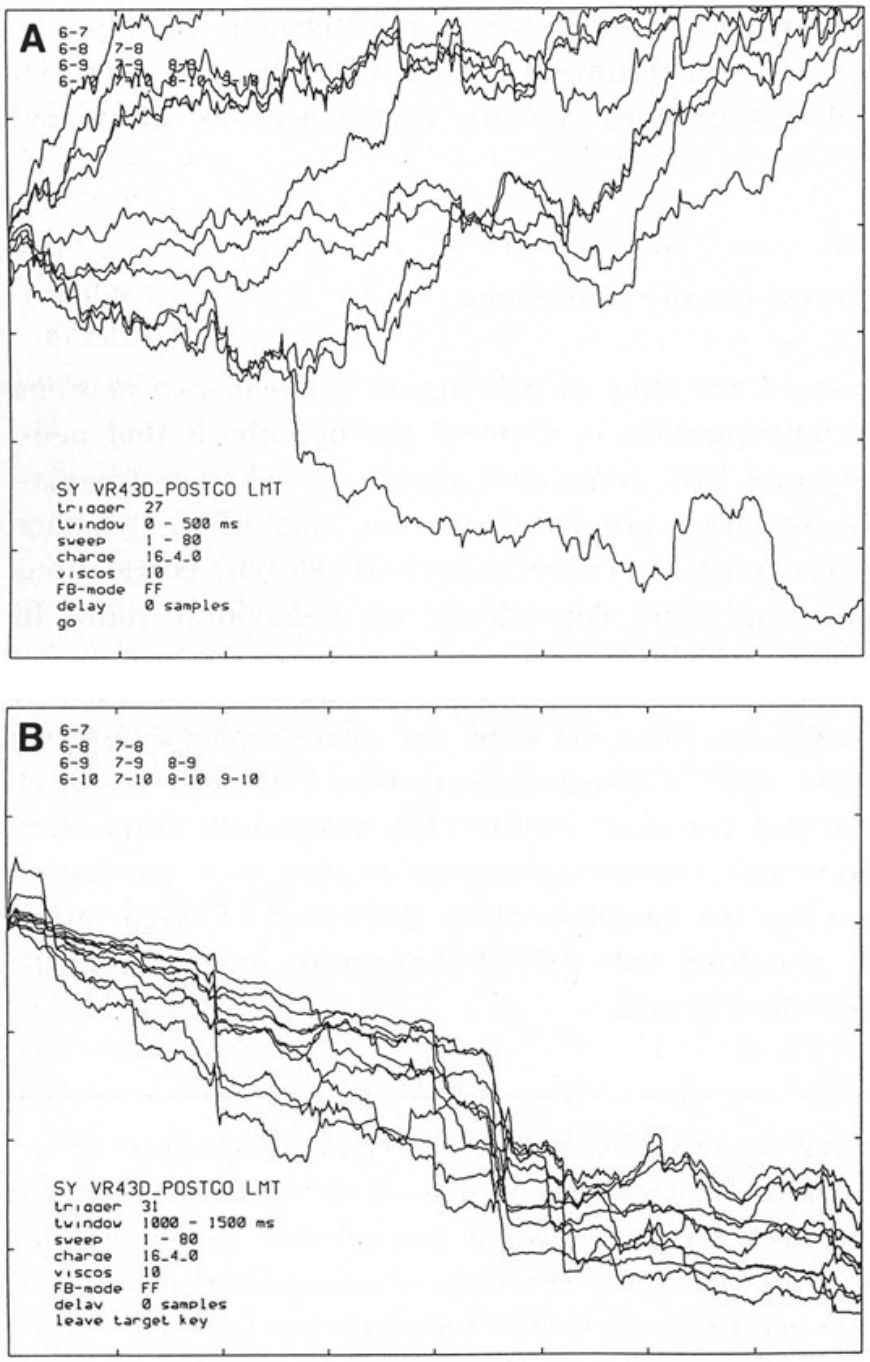


Fig. 12. Modification of interactions among groups of neurons in relation to behavioral state. 'Gravitational Clustering' analysis of correlation among the activities of 5 neurons in the frontal cortex of a monkey during performance of the 'delayed localizing task'. Each set of curves represents the group correlations during a particular sequence of 0.5 second long intervals of spike activity, parsed from a single recording session, the difference being that the first series of intervals (**A**) was time-locked to the GO-signal, while the second series (**B**) was time-locked to the behavioral event of the monkey leaving the target key. Clearly the clustering patterns and, hence, the organization of correlation are distinctly different in these two cases, showing that correlations among groups of neurons in frontal cortex may be altered drastically and in rapid succession, depending on the stimulus context and behavioral state of the animal. Further explanation in text.

Suppose we measure spike trains from N neurons. Each one of these N neurons is represented by a point particle in a fictitious N-space. To each such particle, we associate a time-varying 'charge', determined by the respective neuron's spike train. As a result, the particles will mutually exert forces that cause them to 'move'. The charge functions are defined such that the forces lead to aggregation of those particles which correspond to coherently firing neurons, with each single cluster signifying the member neurons of a particular cell assembly. The time dependence of clustering conveys information on the static ('strength') as well as the dynamic aspects of coherent activity. The resulting configurations can be investigated directly by resorting to high-dimensional cluster analysis techniques, or visually, by appropriate projection of the N-space onto a more convenient 2-space representation. If cell assemblies are dynamic entities, related to stimulus context or behavioral state, the particles associated with the member neurons of such an assembly would aggregate during the stage which calls the assembly to action, and move away from each other to regroup in different clusters, when other assemblies are called upon the stage.

Preliminary results from gravitational analysis of frontal cortex recordings indicate that (a) global correlations among larger groups of neurons in frontal cortex do exist, and that (b) these group correlations may indeed be altered drastically and in rapid succession, depending on the stimulus context and behavioral state of the animal. An example of such group correlation and its behavioral dependence is given in Figure 12. The plots show the pairwise inter-particle distance in the gravitational representation as a function of time, with each single curve representing the firing correlation among a particular pair in the set of simultaneously recorded neurons. The temporal development of clustering is signified by a downward slope of some of the curves: the larger the downward slope, the stronger the positive correlation (and upward for negative correlation). The two panels represent the firing correlations among five well isolated single frontal cortex neurons, recorded simulteously during performance of the localization task. Each of the two panels corresponds to a particular sequence of 0.5 second time intervals of spike activity that were collected from a single recording session. The two panels differ in that the respective time sections were time-locked to different stimulus or behavioral events: similarly to the results in Fig. 11, Fig. 12A describes the correlations during the 0.5 second immediately following the GO-signal, while Fig.

12B covers the interval between 1 and 1.5 second after the monkey's hand left the target key to return to its resting position. Observe how the clustering patterns (and hence, the group correlations) are distinctly different in these two cases. Following the GO-signal (Fig. 12A), only one pair of neurons shows positive correlation (the single descending curve), whereas the remaining particles either remain noisily stationary (i.e. no correlation between the corresponding neurons) or even have a weak tendency to diverge, suggesting a negative correlation. In contrast, during the return movement (Fig. 12B) *all* curves exhibit a strongly similar descent, indicating a collective aggregation into a single cluster. Evidently, during this second interval *all* five neurons temporarily join into a common mode of coherent firing; further analysis (not shown here) reveals that both immediately before and after this particular 0.5 second interval, this collective behavior is very much weaker or altogether absent. It should be born in mind that the selected time sections were separated on the average by only about 1-1.5 second, so that indeed this change of correlation is a very rapid one.

These and similar results (Aertsen and Gerstein 1991; Vaadia et al. 1991) imply that the observed changes in correlation are not simply due to task-related changes in single neuron firing rates, but rather reflect interesting, task-related and highly dynamic changes of interaction among these neurons. We stress that the changes in assembly organization, signified by these changes in firing correlation, could not have been revealed by any single unit analysis of the individual neurons involved.

Conclusion

1. Interactions between neuron pairs as well as between larger groups of neurons can be modified in relation to external events, like sensory stimuli, or to the behavioral state. Such modification may occur on a very short time scale, within a fraction of a second.
2. The activities of pairs of cortical neurons may exhibit rapid modulations of discharge synchronization, that are related to the behavioral state. These modulations may switch the neurons' firing behaviour from being mutually incoherent into a particular coherent state of joint synchrony, or, alternatively, from one particular

pattern of mutual coherence into a different one. Each such pattern may last for only a few tens to hundreds of milliseconds.

3. The modulations in synchronized firing between pairs of cortical neurons may follow a time course which is independent of the firing rate profiles of any of the single neurons involved.

Discussion

Most of the above results could not possibly have been predicted from single neuron measurements. Nevertheless, studies of functional properties of single neurons are still very important. They provide a range of important parameters for each element in the hypothetical 'neuronal network' (maximal rate, response properties, statistical properties of the spike train, etc.). In addition, they provide a description of the functional organization of the cerebral cortex. Thus, single-unit studies can tell us where and when certain processes take place. Moreover, a research strategy that combines the study of the individual properties of single neurons with an analysis of the relations they have with each other allows for a confrontation of different hypotheses, using the same experimental data.

Our observations support the hypothesis that several different neural encoding schemes may be operative in the cortex simultaneously. We postulate that the neural code for higher brain function resides both in the firing activities of single neurons, as well as in the coherent activity of groups of neurons. Our findings further suggest that these 'neuronal groups' are dynamic entities, defined not only by anatomical connections, but also by the everchanging level of correlation among the activities of their member neurons. The salient result of direct observation of the activity in groups of neurons in the working cortex is that the interactions among these neurons may be *context-dependent* and *dynamic* on several different time scales. This suggests that the usual concept of neurons with static interconnections of fixed or only slowly changing efficacy (during learning, for example) is no longer adequate. Instead, we should distinguish between *structural* (or anatomical) connectivity on the one hand, and *functional* (or effective) connectivity on the other. Whereas the former can be described as (quasi) stationary, the latter may be highly dynamic, with

time constants of modulation in the range of tens to hundreds of milliseconds. Thus, it appears that dynamic cooperativity is an emergent property of neuronal assembly organization in the brain.

We hypothesize that the cooperativity and the degree of synchronization among cortical neurons can control the synaptic efficacy of the connections between them. This hypothesis predicts that the effectiveness of interactions among neurons may depend on environmental or internal factors that change the degree of synchronization. Considering that a neuron in the cortex makes contacts with thousands of other cells (Braitenberg and Schüz 1991), it becomes evident that when such a neuron is momentarily co-activated with one set of cells, part of its connections will become effective for a corresponding brief period of time. However, when some time later, due to a change in stimulus context or behavioral state, the same cell is co-activated with another set of neurons, a partly or even altogether different subset of its connections will become effective. Thus, there is no need for the synaptic contacts to be particularly strong: the corresponding connections become effective through synchronous activity with other neurons (Abeles 1982a, 1991). Computer simulations (Erb et al. 1986, 1989, 1990) and analytical calculations (Aertsen and Preissl 1991) on artificial neural networks with various types of architectures have demonstrated that considerable and rapid changes in effective connectivity may, in fact, occur without any associated changes in anatomical connectivity. Rather, such changes in effective connectivity may be a reflection of the dynamics of the activity in the entire network, both regarding the rates (Boven and Aertsen 1990) and the internal coherence (Bedenbaugh et al. 1988, 1990) of firing. Thus, the highly dynamic interplay of activity and connectivity in the cortex gives rise to an ongoing process of functional reorganization. Everchanging groups of neurons, each one recruited for brief periods of time, become co-activated and again de-activated, following each other in rapid succession. It is our conjecture that this dynamic reorganization provides the mechanism which underlies our capacity to rapidly change our sensory perceptions, motor behaviour and sensori-motor associations.

Acknowledgements

The results reported in this paper are based on experiments and analyis performed in the Dept. of Physiology at the Hebrew University in Jerusalem. The contributions by Moshe Abeles, Ehud and Merav Ahissar, Hagai Bergman, Benny Karmon, Yizhar Lavner, Eyal Margalit and Israel Nelken are gratefully acknowledged. In the context of a joint research project, additional analysis was carried out at the Max-Planck-Institut für biologische Kybernetik in Tübingen; we thank Stefan Rotter for his contribution. This research received support from the United States-Israel Binational Science Foundation (grant # 88-00250/1), the German Ministry for Science and Technology (BMFT), the German-Israel Foundation for Research and Development (GIF), and the Graduiertenkolleg Neurobiologie Tübingen. In the context of this joint research project, one of the authors (AA) spent the year 1990-91 on sabbatical leave in the Dept. of Physiology at the Hebrew University; this stay was supported by the Lady Davis Foundation and the Minerva Foundation.

References

Abeles M, Assaf J, Gottlieb Y, Hodis H, Vaadia E (1975) Speculation on a neural substrate for immediate memory. Sensory Physiology and Behavior 15:117-126

Abeles M, Goldstein MH (1977) Multiple spike train analysis. Proc. IEEE 65:762-773

Abeles, M. (1982a) Local cortical circuits. An electrophysiological study. Springer, Berlin,

Abeles M (1982b) Quantification, smoothing, and confidence limits for single units' histograms. J Neurosci Meth 5:317-325

Abeles M (1983) The quantification and graphic display of correlations among three spike trains. IEEE Trans Biomed Engin BME-30:236-239

Abeles M, de Ribaupierre F, de Ribaupierre E (1983) Detection of single unit responses which are loosely time-locked to a stimulus. IEEE Trans Syst Man Cyber SMC-13:683-691

Abeles M, Gerstein GL (1988) Detecting spatiotemporal firing patterns among simultaneously recorded single neurons. J Neurophysiol 60:909-924

Abeles M, Vaadia E, Bergman H (1990) Firing patterns of single units in the prefrontal cortex and neural network models. Network 1:13-35

Abeles M (1991) Corticonics. Neural circuits in the cerebral cortex. Cambridge University Press, Cambridge, UK

Aertsen AMHJ, Gerstein GL (1985) Evaluation of neuronal connectivity: sensitivity of cross correlation. Brain Res 340:341-354

Aertsen A, Gerstein G, Johannesma, P (1986) From neuron to assembly: Neuronal organisation and stimulus representation. In: Palm G, Aertsen A (eds) Brain Theory. Springer, Berlin, pp 7-24

Aertsen A, Bonhoeffer T, Krüger J (1987) Coherent activity in neuronal populations: analysis and interpretation. In: Caianiello, ER (ed) Physics of Cognitive Processes. World Scientific Publishing, Singapore, pp 1-34

Aertsen AMHJ, Gerstein GL, Habib MK, Palm G (1989) Dynamics of neuronal firing correlation: modulation of "effective connectivity". J Neurophysiol 61:900-917

Aertsen AMHJ, Gerstein GL (1991) Dynamic aspects of neuronal cooperativity: fast stimulus-locked modulations of 'effective connectivity'. In: Krüger J. (ed) Neuronal Cooperativity. Springer, Berlin, p 52-67

Aertsen A, Preissl H (in press, 1991) Dynamics of activity and connectivity in physiological neuronal networks. In: Schuster H (ed) Nonlinear dynamics and neuronal networks. VCH Verlag, Weinheim

Ahissar E, Vaadia E (1990) Oscillatory activity of single units in a somatosensory cortex of an awake monkey and their possible role in texture analysis. Proc Natl Acad Sci USA 87:8935-8939

Ahissar M, Ahissar E, Bergman H, Vaadia E (1992) Encoding of sound source location and movement: activity of single neurons and interaction between adjacent neurons in the monkey auditory cortex. J Neurophysiol (in press)

Allum JHJ, Hepp-Reymond MC, Gysin R (1982) Cross-correlation analysis of interneuronal connectivity in the motor cortex of the monkey. Brain Res 231:325-334

Amit D (1989) Modeling brain function. Cambridge University Press, Cambridge, UK

Barlow HB (1972) Single units and sensation: A neuron doctrine for percepteral psychology. Perception 1:371-394.

Bedenbaugh PH, Gerstein GL, Boven K-H, Aertsen AMHJ (1988) The meaning of stimulus dependent changes in cross correlation between neuronal spike trains. Soc Neurosci Abstr 14:651

Bedenbaugh PH, Gerstein GL, Aertsen AMHJ (1990) Dynamic convergence in neural assemblies. Soc Neurosci Abstr 16:1224

Bialek W, Rieke F, de Ruyter van Steveninck R, Warland D (1991) Reading a neural code. Science 252:1854-1857

Boven K-H, Aertsen A (1989) Dynamics of activity in neuronal networks give rise to fast modulations of functional connectivity. In: Eckmiller R et al. (eds) Parallel processing in neural systems and computers. Elsevier Science Publishers, pp 53-56

Braitenberg V (1978) Cell assemblies in the cerebral cortex. In: Heim R, Palm G (eds) Theoretical Approaches to Complex Systems. Lecture Notes in Biomathematics, Vol. 21. Springer, Berlin Heidelberg New York, pp 171-188

Braitenberg V, Schüz A (1991) Anatomy of the cortex. Statistics and geometry. Springer, Berlin

Butters N, Pandya D (1969) Retention of delayed alternation : Effect of selective lesions of sulcus principalis. Science 165:1271-1273

Dayhoff JE, Gerstein GL (1983) Favored patterns in spike trains. I. Detection. J Neurophysiol 49:1334-1348

Dayhoff JE, Gerstein GL (1983) Favored patterns in spike trains. II. Application. J Neurophysiol 49:1349-1363

Deeke L, Kornhuber HH, Lang W, Lang M, Shreiber H (1985) Timing function of the frontal cortex in sequential motor cortex in motor and learning tasks. Human Neurobiol 4:143-154

Dickson JW, Gerstein GL (1974) Interactions between neurons in auditory cortex of the cat. J Neurophysiol 37:1239-1261

Donchin E (ed) (1984) Cognitive Psychophysiology. The Carmal Conferences. Vol. 1. Erlbaum Pub., New Jersey

Eckhorn R, Bauer R, Jordan W, Kruse W, Munk M, Reitboeck HJ (1988) Coherent oscillations: a mechanism of feature linking in the visual cortex? Multiple electrode and correlation analysis in the cat. Biol Cybern 60:121-130

Eckhorn R, Reitboeck HJ, Arndt M, Dicke P (1990) Feature linking via a synchronization among distributed assemblies: simulations of results from cat visual cortex. Neural Computation 2:293-307

Eckhorn R (1991) Stimulus-specific synchronisations in visual cortex: linking features into global figures? In: Krüger J (ed) Neural Cooperativity. Springer, Berlin Heidelberg New York, pp 184-219

Edelman GM (1981) Group selection as the basis for higher brain function. The organization of the cerebral cortex. In: Proc of a neuroscience research program colloquium. Schmitt et. al. (eds) The MIT Press, Cambridge, pp 536-563

Eggermont JJ (1990) The correlative brain. Theory and experiment in neural interaction. Springer, Berlin

Eggermont JJ, Epping WJM, Aertsen AMHJ (1983) Stimulus dependent neural correlations in the auditory midbrain of the grassfrog (Rana temporaria L.). Biol Cybern 47:103-117

Erb M, Palm G, Aertsen A, Bonhoeffer T (1986) Functional versus structural connectivity in neuronal nets. In: Strukturbildung und Musteranalyse, Proc. 9th Cybernetics Congress (DGK) Göttingen (FRG), p 23

Erb M, Aertsen A, Palm G (1989) Functional connectivity in neuronal systems: context-dependence of effective network organization does not require synaptic plasticity. In: Elsner N, Singer W (eds) Dynamics and plasticity in neuronal systems. Thieme, Stuttgart, New York, p 445

Erb M, Aertsen A, Palm G (1990) Stability in physiology-oriented neuronal network models. In: Elsner N, Roth G (eds) Brain - Perception - Cognition. Thieme, Stuttgart, New York, p 527

Evarts EV, Shinoda Y, Wise SP (1984) Neurophysiological approach to higher brain function. Wiley Intersciences Press, New York

Frostig R, Gottlieb Y, Vaadia E, Abeles M (1983) The effects of stimuli on the activity and functional connectivity of local neuronal groups in the cat auditory cortex. Brain Res 272:211-221

Frostig R, Frostig Z, Frysinger R, Schechtman V (1985) Multineuron analysis reveals complex patterns of interaction among neurons. Soc Neurosci Abstr 11:1020

Fuster JM (1973) Unit activity in the prefrontal cortex during delayed response performance: neuronal correlates of transient memory. J Neurophysiol 36:61-78

Fuster JM (1989) The prefrontal cortex. Anatomy, physiology, and neuropsychology of the frontal lobe. Raven Press, New York

Gassanov UG, Galashina AG, Bogdanov AV (1980) A study of neuron systems activity in learning. Neural Mechanisms of Goal-Directed Behavior and Learning 341-352

Gerstein GL, Bloom MJ, Espinosa IE, Evanczuk S, Turner MR (1983) Design of a laboratory for multi-neuron studies. IEEE Trans Systems, Man and Cybernetics SMC-13:668-676

Gerstein G, Perkel D, Dayhoff J (1985) Cooperative firing activity in simultaneously recorded populations of neurons: detection and measurement. J Neurosci 5:881-889

Gerstein G, Aertsen A (1985) Representation of cooperative firing activity among simultaneously recorded neurons. J Neurophysiol 54:1513-1527

Gerstein GL (1988) Information flow and state in cortical neural networks: Interpreting multi-neuron experiments. In: von Seelen W, Shaw G, Leinhos UM (eds) Organization of neural networks. VCH Verlag, Weinheim (FRG), pp 53-75

Gerstein GL, Bedenbaugh P, Aertsen AMHJ (1989) Neuronal Assemblies. IEEE Trans on Biomed Engin 36:4-14

Georgopoulos AP, Kettner RE, Schwartz AB (1988) Primate motor cortex and free arm movements to visual targets in three-dimensional space. II. Coding of the direction of movement by a neuronal population. J Neurosci 8:2928-2937

Georgopoulos AP, Lurito JT, Petrides M, Schwartz AB, Massey JT (1989) Mental rotation of the neuronal population vector. Science 243:234-236

Gielen CCAM, Hesselmans GHFM, Johannesma PIM (1988) Sensory interpretation of neural activity patterns. Math Biosci 92:15-35

Goldberg ME, Segraves MA (1987) Visuospatial and motor attention in the monkey. Neuropsychologia 25(1A):107-118

Goldman PS, Nauta WJH (1977) Columnar distribution of cortico-cortical fibers in the frontal association, limbic and motor cortex of the developing Rhesus monkey. Brain Res 122:393-413

Goldman-Rakic PS (1987) Circuitry of primate prefrontal cortex and the regulation of behavior by representational knowledge. In: Mountcastle VB, Plum F (eds) The Nervous System, Vol. V, Handbook of Physiology. Am Physiol Soc, Bethesda, MD, pp 373-417

Gottlieb Y, Vaadia E, Abeles M (1989) Single unit activity in the auditory cortex of a monkey performing a short term memory to tones task. Exp Brain Res 74:139-148

Gray CM, Singer W (1989) Stimulus-specific neuronal oscillations in orientation columns of cat visual cortex. Proc Natl Acad Sci USA 86:1698-1702

Gray CM, König P, Engel AK, Singer W (1989) Oscillatory responses in cat visual cortex exhibit inter-columnar synchronisation which reflects global stimulus properties. Nature 388:334-337

Hebb D (1949) The organization of behavior. A neuropsychological theory. Wiley, New York

Hesselmans GHFM, Johannesma PIM (1989) Spectro-temporal interpretation of activity patterns of auditory neurons. Math Biosci 93:31-51

Hopfield JJ (1982) Neuronal networks and physical systems with emergent collective computational abilities. Proc Natl Acad Sci USA, 79:2554-2556

Hopfield JJ and Tank DW (1986) Computing with neural circuits: A model. Science 233:625-633

Hubel DH, Wiesel TN (1968) Receptive fields and functional architecture of monkey striate cortex. J Physiol 195:215-243

Hubel DH, Wiesel TN (1977) Functional architecture of macaque monkey visual cortex (Ferrier Lecture). Proc Roy Soc London, Vol. B. 198:1-59

Johannesma PIM (1981) Neural representation of sensory stimuli and sensory interpretation of neural activity. In: Szekely Gy, Labos E, Damjanovich S (eds) Neural communication and control. Adv Physiol Sci 30:103-125

Johannesma P, Aertsen A, van den Boogaard H, Eggermont J, Epping W (1986) From synchrony to harmony: Ideas on the function of neural assemblies and on the interpretation of neural synchrony. In: Palm G, Aertsen A (eds) Brain Theory. Springer, Berlin Heidelberg New York, pp 25-47

König P, Schillen TB (1991) Stimulus-dependent assembly formation of oscillatory responses. 1: Synchronisation. Neural Computation 3:155-167

Krüger J (1983) Simultaneous individual recordings from many cerebral neurons: techniques and results. Rev Physiol Biochem Pharmacol 98:177-233

Krüger J, Aiple F (1988) Multimicroelectrode investigation of monkey striate cortex: spike trains correlations in infragranular layers. J Neurophysiol 60(2):798-828

Krüger J (1991) Spike train correlations on slow time scales in monkey visual cortex. In: Krüger J (ed) Neuronal Cooperativity. Springer, Berlin, pp 105-132

Lavner Y (1989) Functional interactions between cells in the prefrontal cortex of behaving monkeys. M.Sc. Thesis (in Hebrew), Hebrew University, Jerusalem

Lee C, Rohrer WH, Sparks DL (1988) Population coding of saccadic eye movements by neurons in the superior colliculus. Nature 332:357-360

Legendy C, Salcmann M (1985) Bursts and recurrences of bursts in the spike trains of spontaneously active striate cortex neurons. J Neurophysiol 53:926-939

Lurito JT, Schwartz AB, Petrides M, Kettner RE, Georgopoulos AP (1988) Crosscorrelations between motor cortical cells simultaneously recorded during reaching task in the monkey. Soc Neurosci Abst 14:142.5

Moore GP, Perkel DH, Segundo JP (1966) Statistical analysis and functional interpretation of neuronal spike data. Ann Rev Physiol 28:493-522

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

Mountcastle VB (1957) Modality and topographic properties of single neurons of cat's somatic sensory cortex. J Neurophysiol 20:408-434

Mountcastle VB (1977) An organizing principle for cerebral function: the unit module and the distributed system. In: Edelman GM, Mountcastle VB (eds) The Mindful Brain. MIT Press, Cambridge (MA), pp 7-50

Murphy JT, Kwan HC, Wong YC (1985) Cross-correlation studies in primate motor cortex: Synaptic interaction and shared input. Can J Neurol Sci 12:11-23

Neven H, Aertsen A (1992) Rate coherence and event coherence in the visual cortex: a neuronal model of object recognition (submitted)

Niki H, Watanabe M (1976) Pre-frontal unit activity and delayed response: Relation to cue location versus direction of response. Brain Res 105:79-88

Niki H, Watanabe M (1979) Prefrontal and cingulate unit activity during timing behavior in the monkey. Brain Res 171:213-224

Optican LM, Richmond B (1987) Temporal encoding of two-dimensional patterns by single units in primate inferior temporal cortex. III. Information theoretic analysis. J Neurophysiol 57:162-178

Palm G (1982) Neural assemblies. An alternative approach to artificial intelligence. Springer, Berlin

Palm G, Aertsen A (1986) Brain Theory. Springer, Berlin

Palm G, Aertsen AMHJ, Gerstein GL (1988) On the significance of correlations among neuronal spike trains. Biol Cybern 59:1-11

Passingham RE (1975) Delayed matching after selective prefrontal lesions in monkeys (macaca mulata). Brain Res 92:89-102

Perkel DH, Gerstein GL, Moore GP (1967) Neuronal spike trains and stochastic point processes. II. Simultaneous spike trains. Biophys J 7:419-440

Perkel DH, Bullock TH (1968) Neural Coding. Neurosci Res Progr Bull Vol. 6

Perkel DH, Gerstein GL, Smith M, Tatton WG (1975) Nerve-impulse patterns: a quantitative display technique for three neurons. Brain Res 100:271-296

Perrett DI, Rolls ET, Caan W (1982) Visual neurons responsive to faces in monkey temporal cortex. Exp Brain Res 47:329-342

Petrides M (1986) The effect of periarcuate lesions in the monkey on performance of symmetrically and asymmetrically reinforced and auditory go, no-go tasks. J Neurosci 6:2054-2063

Richmond BJ, Optican LM (1987) Temporal encoding of two-dimensional patterns by single units in primate inferior temporal cortex. II. Quantification of response waveform. J Neurophysiol 57:147-161

Rumelhart DE, McClelland JL, and the PDP Research Group (1986) Parallel distributed processing. Explorations in the microstructure of cognition. MIT Press, Cambridge, Mass.

Schillen TB, König P (1991) Stimulus-dependent assembly formation of oscillatory responses. 2: Desynchronisation. Neural Computation 3:167-178

Sompolinsky H, Golomb D, Kleinfeld D (1990) Global processing of visual stimuli in a network of coupled oscillators. Proc Natl Acad Sci USA 87:7200-7204

Sompolinsky H, Golomb D, Kleinfeld D (1991) Cooperative dynamics in visual processing. Physical Rev A 43:6990-7011

Sporns O, Gally JA, Reeke GN Jr, Edelman GM, (1989) Reentrant signaling among simulated neuronal groups leads to coherency in their oscillatory avtivity. Proc Natl Acad Sci USA 86:7265-7269

Stevens JK, Gerstein GL (1976) Interactions between cat lateral geniculate neurons. J Neurophysiol 39:239-256

Toyama K, Kimura M and Tanaka K (1981) Crosscorelation analysis of interneuronal connectivity in cat visual cortex. J Neurophysiol 46:191-201

Vaadia E, Benson DA, Hienz RD, Goldstein MH, Jr. (1986) Unit study of monkey frontal cortex: active localization of auditory and visual stimuli. J Neurophysiol 56:934-952

Vaadia E, Abeles M (1987) Temporal firing patterns of single units, pairs and triplets of units in the auditory cortex. J Isr Med Sci 23:75-83

Vaadia E, Kurata K, Wise SP (1988) Neuronal activity preceding directional and nondirectional cues in the premotor cortex of rhesus monkeys. Somatosensory and Motor Res 6:207-2309

Vaadia E, Bergman H, Abeles M (1989) Neuronal activities related to higher brain functions - theoretical and experimental implications. IEEE Trans on Biomed Engin 36:25-35

Vaadia E, Ahissar E, Bergman H, Lavner Y (1991) Correlated activity of neurons: a neural code for higher brain functions? In: Krüger J (ed) Neuronal Cooperativity. Springer, Berlin, p 249-279

van Gisbergen JAM, van Opstal AJ, Tax AA (1987) Collicular ensemble coding of saccades based on vector summation. Neurosci 21:541-555

Vogels R (1990) Population coding of stimulus orientation by striate cortical cells. Biol Cybern 64:25-31

von der Malsburg C (1981) The correlation theory of brain function. Internal report 81-2. Max-Planck-Institute for Biophysical Chemistry, Göttingen (FRG)

von der Malsburg C (1986) Am I thinking assemblies? In: Palm G, Aertsen A (eds) Brain Theory. Springer, Berlin Heidelberg New York, pp 161-176

Watanabe M (1986a) Prenatal unit activity during delayed conditional go/nogo discrimination in monkey I. Relation to stimulus. Brain Res 382:1-14

Watanabe M (1986b) Prefrontal unit activity during delayed conditional go/nogo discrimination in monkey II. Relation to go and nogo responses. Brain Res 382:15-27

Wise SP, Mauritz KH (1985) Set related neuronal activity in the premotor cortex of rhesus monkeys: effects of changes in motor set. Proc R Soc Lond B 223:331-354