Rhythmic and patterned neuronal firing in visual cortex

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We present evidence from multi-electrode recordings that the stimulus driven activity in a region of monkey visual cortex displays synchronous, oscillatory behaviour with temporally changing patterns of firing. The spatial-temporal patterns are dependent on cortical layer and on visual stimulus, 'build up and die down' with a period of 70–100 msec, and cannot be factorized into separate spatial and temporal components. This finding supports neural network models which explicitly incorporate spatial-temporal structure, ruling against a purely spatial code for information processing. The new type of analysis presented here is also suitable for direct on-line interactive analysis during multi-electrode recording experiments. Further, it could be modified for use in human EEG or evoked response recordings. [Neurol Res 1993; **15**: 46–50]

Keywords: Multi-electrode analysis; visual cortex; synchronous firing; spatial-temporal code; neural networks

INTRODUCTION

The key to distinguishing between the various neural network models of cortical function is to simultaneously observe the firing of a number of neurons in the cortex. Here, using a new type of analysis, we present evidence from experimental observations of multi-electrode recordings[1–3] which support models that explicitly incorporate spatial–temporal structure in their 'code' for information processing. Neural network models of cortical function contrast widely in their basic assumptions concerning the code of information processing[4]. In particular, we distinguish 1) a localized spatial code[5] (with 'grandmother' cells as a limiting case), 2) a distributed spatial code[6–15], including spin-glass models[12,13], 3) a localized spatial–temporal code in a manner suggested by the Mountcastle[16] organizational principle for the cortical column (about 700 μ diameter), embodying activity patterns moderately localized in space and time, and 4) a distributed spatial-temporal code such as embodied in the Hebbian cell assembly[17]. An example of type 3) is the trion model[18,19]. It incorporates an idealized subunit, the trion which represents a localized group of about 100 neurons, with three levels of firing activity, and a discrete time step for processing of about 50 ms. The interactions among trions depend on the activity at two previous time steps; they are highly structured, localized, competing, and modifiable by a Hebbian mechanism. Examples of type 4), the distributed neuronal assembly, are described by, e.g., Briatenberg[20] and Palm[21]. Our results give evidence for a spatial–temporal code (model types 3) and 4)) as opposed to a pure spatial code (types 1) and 2)).

The key to understanding the code of higher cortical processing involves looking simultaneously at the appropriate spatial and temporal separations; suggested scales are roughly 100 μ and 25 msec, respectively. At too large a scale, all structure in the firing patterns will be washed out, whereas at too fine a scale, one will be lost in a morass of detail and fluctuations. With this in mind, we employ here a new type of analysis for data from multi-electrode recordings which will readily enable us to observe spatial–temporal structure in the response of the observed cortical network. Furthermore, our analysis can be executed extremely fast and is thus suitable for on-line interactive use during multi-electrode recording experiments. Our new analysis could be modified for use in human EEG or evoked response recordings.

METHODS

Recordings were made[1–3] with 30 microelectrodes (5 × 6 array with 160 μ spacing) from the striate cortex of vervet monkeys (*Cercopithecus aethiops*). The animals were anaesthetized by N_2O and low doses of halothane. The electrode tips lay in a tangential plane. Most electrodes yielded either well-isolated spikes or spikes from one cell slightly contaminated by spikes from neighbouring cells. Among the stimuli applied repeatedly were sequences of large coloured fields (red, green or white) turned on and off with each phase lasting 2 sec.

The new analysis that we employ here is as follows: For each electrode, we determined the time course of firing rate $r(t)$ to each of the colour stimuli, averaged over several presentations (i.e. the classical PSTH; the time axis was divided into bins of 25 msec); in addition we determined the overall average of spike rate R (a single constant) over several repetitions and applications of all three colours. Using Poisson statistics, the chance

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probability for any number of counts in a bin can be determined. Since for high and low counts (compared to the average) these chance probabilities fall off rapidly, the scale of probabilities was subdivided logarithmically into six response magnitudes measuring deviation from the average firing rate R:

Response magnitude:					
−6	−3	0	3	6	9
Probability of deviation:					
$0 \rightarrow 10^{-6}$	$10^{-6} - \rightarrow 10^{-3}$	0.998	$10^{-3} - \rightarrow 10^{-6}$	$10^{-6} - \rightarrow 10^{-9}$	$10^{-9} \rightarrow 0$
Firing rate:					
Far below R		R	Far above R		(1)

The purpose of adopting a magnitude scale is to obtain a probabilistic measure for ring level, i.e., one which emphasizes deviation from expectancy, rather than firing rate per se. As an example, consider a neuron with an average rate of 7.5 counts/bin. The Poisson probability of actually measuring a count of, say, 29 or higher, equals 10^{-9}. According to our scale (1), this highly deviating count would be assigned the response magnitude 9. This logarithmic scale arises from the statistical 'significance' or confidence level (CL) of deviations from a Poisson distribution. The CL of a particular count is defined as the probability of measuring that count or a higher one[22–24]. In the case of 'suppression', it is the probability of finding that count or an even lower one. The response magnitude is defined as $C_T = -\log(\mathrm{CL}/(1 - \mathrm{CL}))$. The CL for a large number of cumulative events becomes a gaussian, and the response magnitude is its exponent:

$$C_T = T(r(t) - R)^2/2r(t)$$

where $r(t)$ and R are defined above and T is the total observation time for a bin (number of trials times the time width of a bin). Note that the quantity C_T/T is independent of the total observation time. The response magnitudes C_T form the basis of our analysis.

RESULTS

Figure 1 shows the response magnitudes C_T based on 40 trials, for a recording from layer IVc in an arrangement corresponding to that of the electrode array. The temporal evolution is shown in 24 time steps of 25 msec each, beginning with 'white on' (*Figure 1a*) and 'green on' (*Figure 1b*), respectively. One observes that (i) the activity builds up and dies down throughout the array with a period of about 3 time steps, (ii) the spatial–temporal distributions are not factorizable, i.e. they are not simply a temporal modulation of a spatial pattern, (iii) the spatial-temporal distributions depend on the nature of the stimulus in a nontrivial manner. *Figure 2* shows the robustness of the pattern in *Figure 1b*: to this end we subdivided the data into two parts by separating the odd numbered trials from the even numbered ones. In order for our new analysis to be useful, the response to a particular stimulus must be 'reproducible'. *Figure 2* is some measure that this is satisfied.

In order to emphasize the temporal evolution of the 'population activity', we show in *Figure 3* the sums of the absolute values of the response magnitudes (divided by the common factor 3) across the entire electrode array as a function of time. We define this new important quantity as the Cortical Array Response Magnitude which will clearly exhibit structure present in the temporal firing response of the entire observed network. The rhythmicity in overall firing of the network in *Figures 1a* and *1b* is now clearly apparent in *Figures 3a* and *3b*: there are six, approximately equidistant,

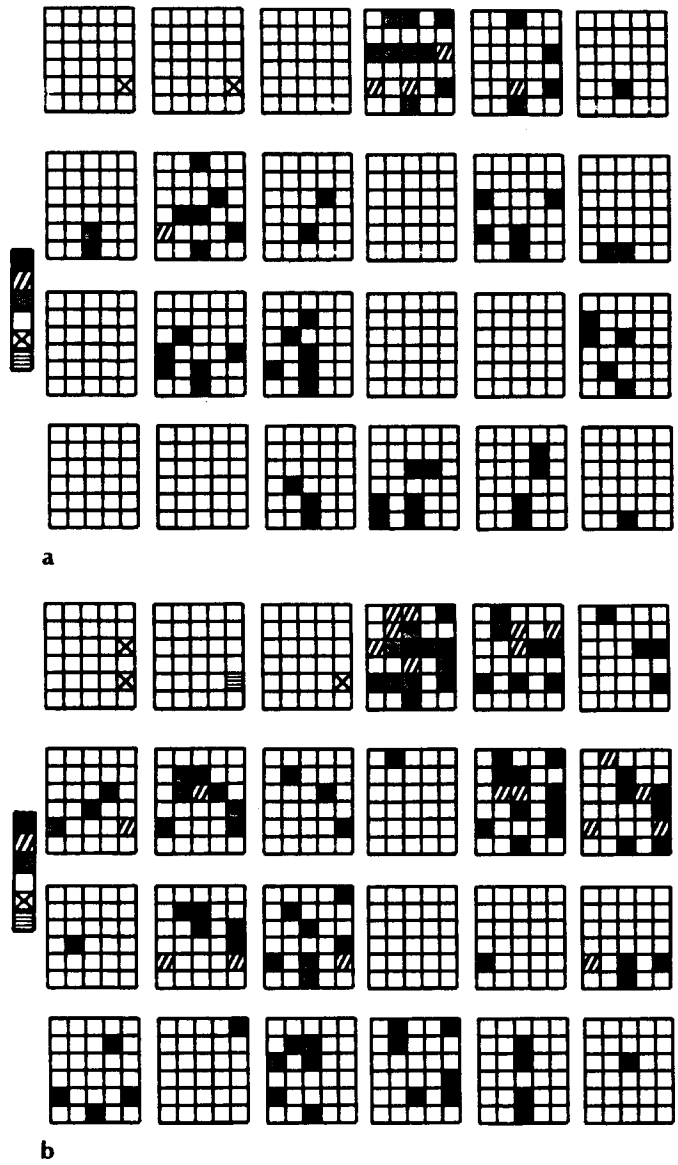


Figure 1: Spatial-temporal distribution of response magnitudes for stimulus-driven activity in layer IVc in visual cortex of the vervet monkey. Each individual coloured square represents the response magnitude, C_T, equation (1) determined for a particular electrode during a time bin of 25 msec; the spatial arrangement of squares in a 5 × 6 matrix corresponds to that of the electrode array (5 × 6 matrix, with 160 μ spacing). The temporal evolution is shown as a series of snapshots from an 'animation movie': 24 frames covering a time span of 600 msec, starting at stimulus onset. Time increases from left to right, and then from top to bottom. The symbol code is indicated by the symbol bar alongside each of the figure elements, with highest activity (response magnitude 9) black, decreasing to average (response magnitude 0) white and lowest (response magnitude −6) horizontal stripes. (**a**) Recordings were made during presentation of a uniform white and (**b**) green stimumus, respectively. Number of trials is 40

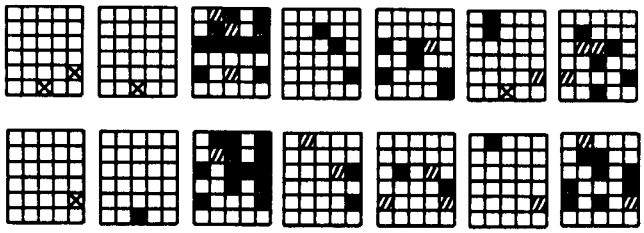


Figure 2: Robustness of the response. Subdividing the available set of 40 trials in *Figure 1b* into two equal parts and comparing the patterns for each of these parts allows us to show the robustness of the response magnitudes. Using bins of 40 msec for comparable statistics we show the response magnitudes for the first 7 time bins determined separately from the subsets of odd numbered trials (top line) and even numbered ones (bottom line). The symbol code is the same as in *Figure 1*.

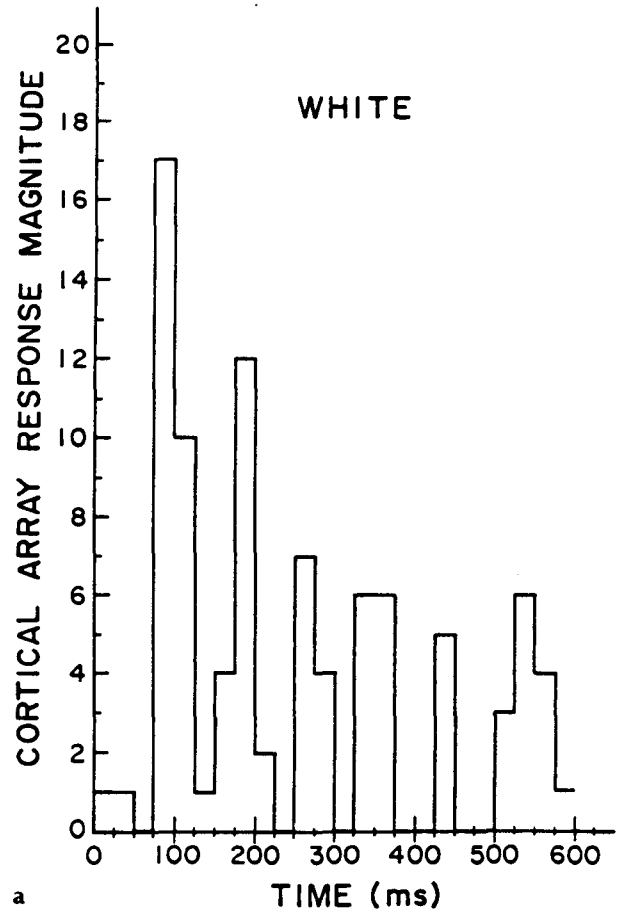
peaks at comparable positions in both curves. Similar results were found in other layers: *Figures 3c* and *3d* show the curves for a recording from layer IVa of the same animal. Note that again the period is slightly above 3 time steps (i.e. 80–90 msec); in addition the peaks are delayed by 25 msec as compared to those in *Figures 3a* and *3b*. *Figure 3e*, finally, shows a similar curve for a recording from layer VI of another animal. Here the interval between peaks is somewhat larger: about 5 time steps, or 125 msec. Note that the curves in *Figure 3* describe the time course of the summated relative firing levels. We found that, for each of these cases A–E, the spatial-temporal pattern is non-factorizable into separate spatial and temporal patterns.

A possible origin of the observed temporal structure is that the activity is circulated vertically among the cortical layers within an area[25,26]. In the trion model[18,19], the dependence of firing activity on the two previous time steps (which yield oscillations) may have the physiological basis of upper and lower cortical layers forming separate trion networks, and excitations being circulated between them. In addition, thalamic circuits[27] as well as interactions among different cortical areas may also play a role in producing rhythmicity.

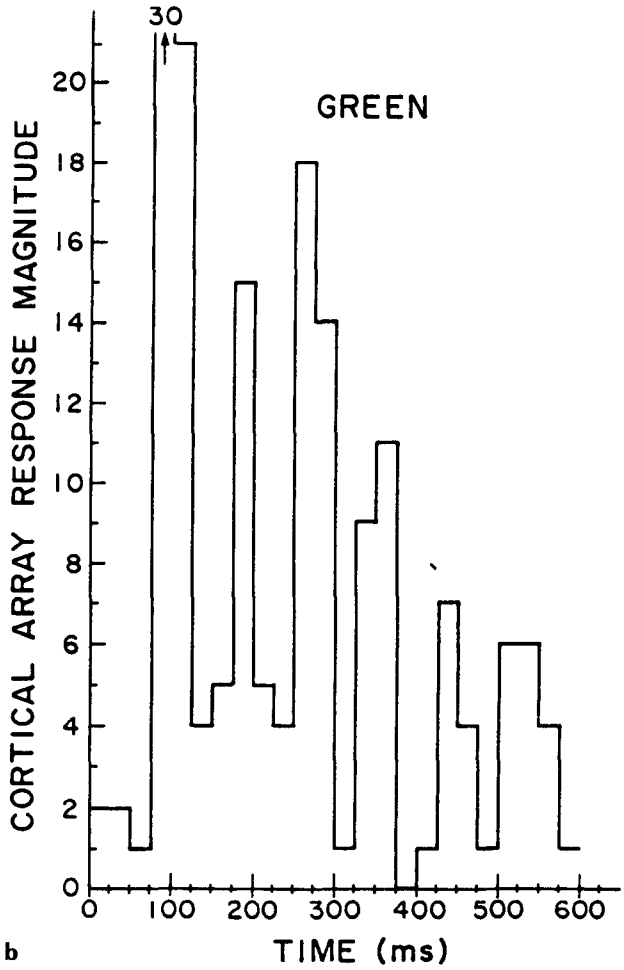
Taking the average over several stimulus repetitions was done to improve statistics and to approximate the sampling of more neurons in postulated localized assemblies ('ergodic' hypothesis[28]). However, since (a) the frequency of 'oscillation' is not necessarily constant during a trial or across trials, and (b) the phase of oscillation is not necessarily rigidly locked to the stimulus, later oscillations, especially, tend to be washed out by averaging (see *Figure 4*). Some of the responses, in particular those to red stimuli, which were interleaved between the green and white stimuli, showed less rhythmic behaviour. This indicates that we are not merely observing the manifestations of a particular autonomic 'brain state' such as sleep (see also refs 29–34).

CONCLUSION

We conclude that the stimulus-driven neuronal activity in a region of monkey visual cortex about the size of a cortical column displays synchronous, oscillatory behaviour. The spatial–temporal patterns determined from our new analysis are layer and stimulus dependent, 'build up and die down' rhythmically with



a



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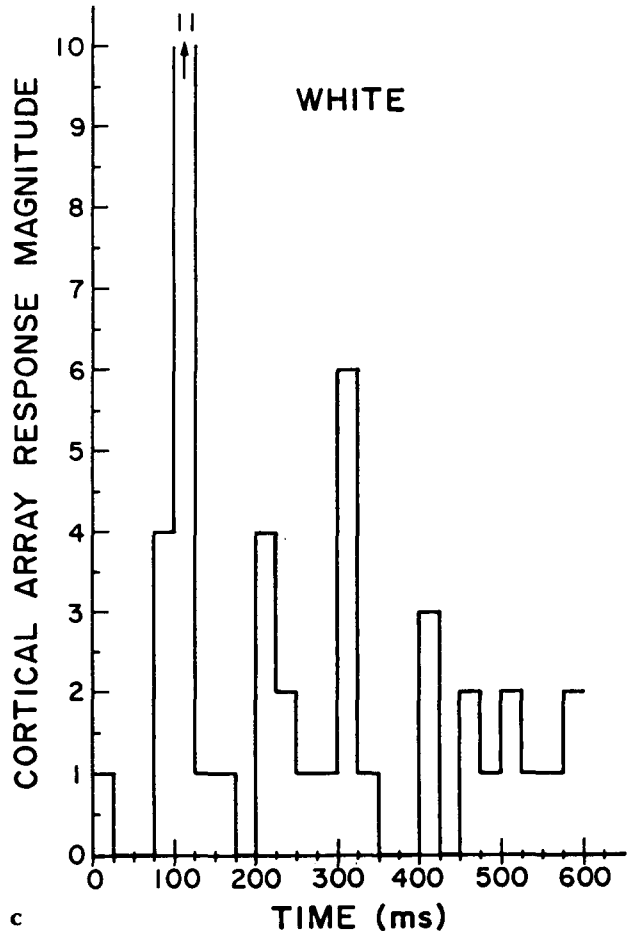

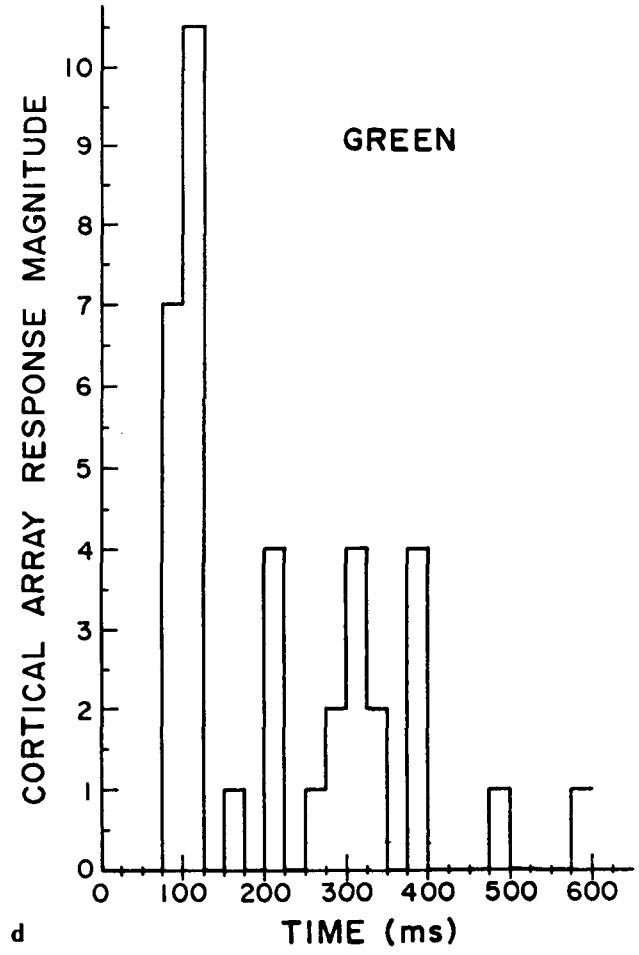

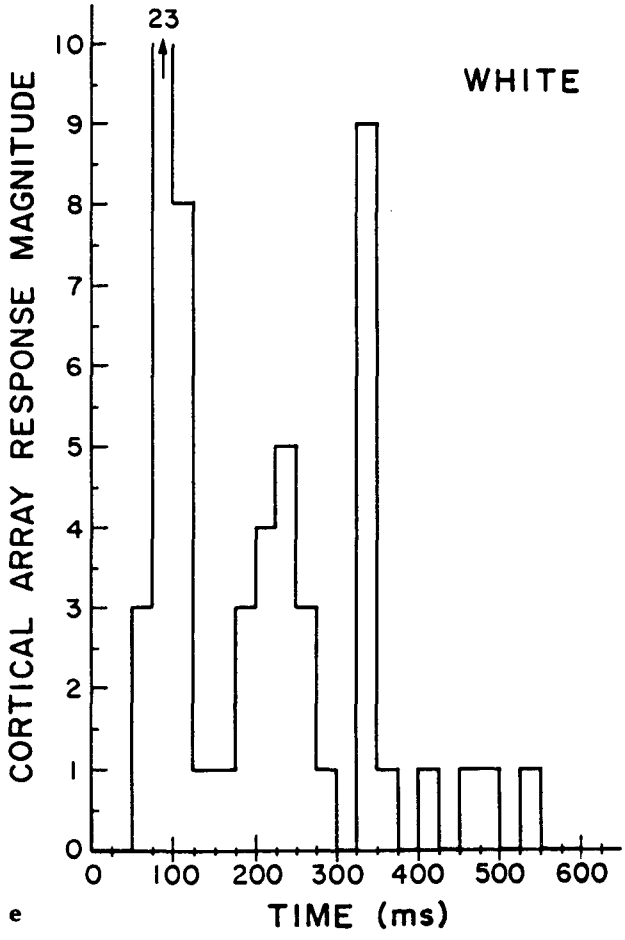

Figure 3: Temporal evolution of strimulus-driven 'population activity' in different layers in visual cortex of the vervet monkey. The Cortical Array Response Magnitude is defined as the sum of the absolute values of the response magnitudes C_r (divided by the common factor 3) over the electrode array (cf. *Figure 1*) as a function of time. (*a*) and (*b*): Time course of cortical array response magnitude for the recordings from layer IVc shown in *Figures 1a* and *1b*, respectively. Note the six, roughly equidistant peaks at comparable positions in both curves. (c) and (*d*): Similar curves for a recording from layer IVa of the same animal for a white (c) and green (*d*) stimulus (number of trials is 40). Again the period is slightly above 3 time bins (i.e. 80–90 msec); note that, in addition, the peaks are delayed by 25 msec as compared to those in (*a*) and (*b*). (*e*): Time course of overall firing level for a recording from layer VI of another animal for a white stimulus (number of trials is 19). Note that in this case the interval between peaks is somewhat larger: about 5 time bins, or 125 msec

periods of 70–100 msec, and cannot be factorized into separate spatial and temporal components. These results give evidence for a spatial–temporal code (model types 3) and 4)) as opposed to a purely spatial code (types 1) and 2)).

In order to understand 'higher brain function', it is important not only to investigate the relationships between neuronal events and external sensory or motor events, but also those among the neuronal events themselves, which underlie the patterns described here. The results presented are a first step in this direction; further experiments accompanied by theoretical considerations are in progress. The program presented here is a considerable step forward in the analysis of multi-electrode data, and can be used in a direct on-line interactive manner during future

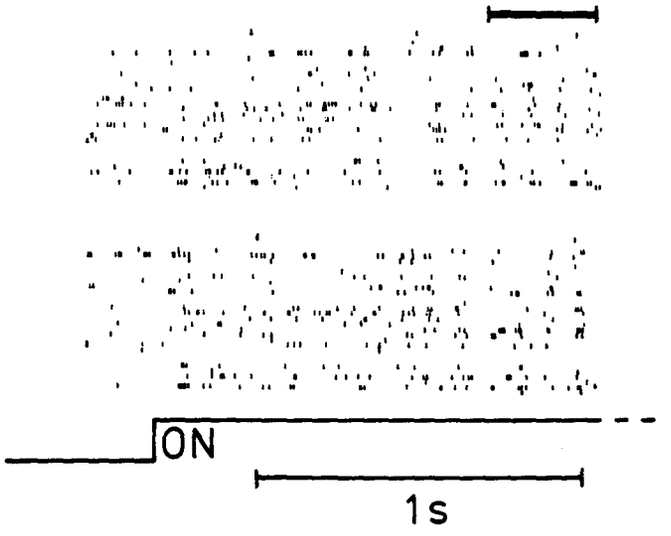

Figure 4: Spike trains from two trials of the 30 neurons shown in *Figure 1a*. The two stripes of dots represent two of the responses to 'white on'; the section shown extends to 1300 msec after stimulus onset. In the time span marked by the horizontal bar at upper right, clear oscillations in firing occur, but in these two trials they are approximately in counterphase; hence in trial averaging they would cancel

experiments. We predict that the use of a chronic implanted array of electrodes in an alert, interested behaving animal along with 'meaningful' stimuli would dramatically enhance the rhythmic, synchronous spatial–temporal patterned responses seen in *Figure 1* that we believe are associated with 'higher' cortical processing. Feedback from higher cortical areas will undoubtedly play an important role in the alert animal.

Finally we suggest that the new type of spatial-temporal analysis presented here might be modified for use in multi-site human EEG and evoked response recordings. Here one would average slow wave amplitudes for each electrode over the time bins. The levels of activity for each site could be determined by the deviations in each time bin from the average as measured by the standard deviation. Just as in the above search for spatial-temporal neuronal patterns in multi-electrode recordings, the usefulness of our suggested analysis based on the response magnitude C_T and the Cortical Array Response Magnitude shown in *Figures 1–3* for the neuronal data requires that the patterns found in these slow wave data must be reproducible and related to the stimuli or mental processes.

REFERENCES

1 Krüger J, Bach M. Simultaneous recording with 30 microelectrodes in monkey visual cortex. *Exp Brain Res* 1981; **41**: 191–194
2 Krüger J, Aiple F. Multimicroelectrode investigation of monkey striate cortex: spike train correlations in the infragranular layers. *J Neurophysiol* 1988; **60**: 798–828
3 Aiple F, Krüger J. Neuronal synchrony in monkey striate cortex: interocular signal flow and dependence on spike rates. *Exp Brain Res* 1988; **72**: 191–194
4 Gerstein GL, Bedenbaugh P, Aertsen AMHJ. Neuronal assemblies. *IEEE Trans Biomed Eng* 1989; **36**: 4–14
5 Ballard DH. Cortical connections and parallel processing: structure and function. *Behav Brain Sci* 1986; **9**: 67–120
6 MacGregor RJ, Lewis ER. *Neural Modeling*. New York: Plenum, 1977
7 Anderson JA, Rosenfeld E, eds. *Neurocomputing*, Cambridge: MIT Press, 1988
8 Hinton GE, Anderson JA, eds. *Parallel Models of Associative Memory*, Hillsdale: Lawrence Erlbaum, 1981
9 Palm G, Aertsen A, eds. *Brain Theory*, Berlin: Springer-Verlag, 1986
10 Di Prisco GV. *Hebb synaptic plasticity. Prog Neurobiol* 1984; **22**: 89–102
11 Kohonen T. *Self-Organization and Associative Memory*, Berlin: Springer-Verlag, 1984
12 Hopfield JJ. Neural networks and physical systems with emergent collective computational abilities. *Proc Natl Acad Sci USA* 1982; **79**: 2554–2558
13 Hopfield JJ, Tank DW. Computing with neural circuits: a model. *Science* 1986; **233**: 625–633
14 von Seelen W, Shaw G, Leinhos UM, eds. *Organization of Neural Networks*, Weinheim: VCH, 1988
15 Shaw GL, Palm G, eds. *Brain Theory Reprint Volume*, Singapore: World Scientific Publishing, 1988
16 Mountcastle VB. An organizing principle for cerebral function: the unit module and the distributed system. In: Edelman GM, Mountcastle VB, eds. *The Mindful Brain*, Cambridge: MIT Press, 1978: pp. 1–50
17 Hebb DO. *The Organization of Behavior*. New York: Wiley, 1949
18 Shaw GL, Silverman DJ, Pearson JC. Model of cortical organization embodying a basis for a theory of information processing and memory recall. *Proc Nat Acad Sci USA* 1985; **82**: 2364–2368
19 Leng X, McGrann JV, Shaw GL. Reversal of epileptic state by patterned stimulation suggested by trion model calculations. *Neurol Res* 1992; **14**: 57–61
20 Braitenberg V. In: Palm G, Aertsen A, eds. *Brain Theory*, 81-96 Berlin: Springer, 1986: pp. 81–96
21 Palm G. *Neural Assemblies*. Berlin: Springer, 1982: pp. ???–???
22 Abeles MJ. Quantification, smoothing and confidence limits for single-units' histograms. *J Neurosc Methods* 1982; **5**: 317–325
23 Feller W. *An Introduction to Probaility Theory and its Applications*, New York: Wiley, 1968
24 Palm G, Aertsen AMHJ, Gerstein GL. On the significance of correlations among neuronal spike trains. *Biol Cybern* 1988; **59**: 1–11
25 Krone G, Mallot H, Palm G, Schuz A. Spatiotemporal receptive fields: a dynamical model derived from cortical architectonics. *Proc R Soc London* 1986; **B226**: 421–444
26 von Seelen W, Mallot HA, Giannakopoulos, F. Characteristics of neuronal systems in the visual cortex. *Biol Cyberg* 1987; **56**: 37–49
27 Andersen P, Andersson SA. Physiological Basis of the Alpha Rhythm, New York: Appleton-Century-Crofts, 1968
28 Shaw GL, Harth E, Scheibel AB. Cooperativity in brain function: assemblies of approximately 30 neurons. *Exp Neurol* 1982; **77**: 324–358
29 Gray CM, Singer W. Stimulus-specific neuronal oscillations in orientation columns of cat visual cortex. *Proc Nat Acad Sci USA* 1989; **86**: 1698–1702
30 Eckhorn R, Bauer R, Jordan W, Brosch M, Kruse W, Munk M, Reitboeck, HJ. Coherent oscillations: a mechanism of feature linking in the visual cortex: Multiple electrode and correlation analysis in the cat. *Biol Cybern* 1988; **60**: 121–130
31 Dinse HR, Kruger K, Best J. A temporal structure of cortical information processing. *Concepts Neurosci* 1990; **1**: 199–238
32 Richmond BJ, Optician LM, Spitzer H. Temporal encoding of two-dimensional patterns by single units in primate primary visual cortex. I. Stimulus-response relations. *J Neurophysiol* 1990; **64**: 351–369
33 Singer W. Search for coherence: a basic principle of cortical self-organization. *Concepts Neurosci* 1990; **1**: 1–26
34 Gray CM, Konig P, Engel AK, Singer W. Oscillatory responses in cat visual cortex exhibit intercolumnar synchronization which reflects global stimulus properties. *Nature* 1989; **338**: 334–337