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Journal

Journal of Neurophysiology, 76(1)

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Publication Date

1996-07-01

Peer reviewed

Spatiotemporal Analysis of Prepyriform, Visual, Auditory, and Somesthetic Surface EEGs in Trained Rabbits

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SUMMARY AND CONCLUSIONS

1. Spatial ensemble averages were computed for 64 traces of electroencephalograms (EEGs) simultaneously recorded from 8×8 arrays over the epidural surfaces of the prepyriform cortex (PPC) and visual, somatic, and auditory cortices. They revealed a common waveform across each array. Examination of the spatial amplitude modulation (AM) of the waveform revealed classifiable spatial patterns in short time segments. The AM patterns varied within trials after presentation of identical conditioned stimuli, and also between trials with differing stimuli.

2. PPC EEGs revealed strong correlates with the respiratory rhythm; neocortical EEGs did not.

3. Time ensemble averaging of the PPC EEG attenuated the oscillatory bursts, indicating that olfactory gamma oscillations (20–80 Hz) were not phase-locked to the times of stimulus delivery but instead to inhalations. Time ensemble averages of neocortical recordings across trials revealed average evoked potentials starting 30–50 ms after the arrival of the stimulus.

4. Average temporal fast Fourier transform (FFT) power spectral densities (PSDs) from pre- and poststimulus PPC EEG segments revealed a peak of gamma activity in olfactory bursts.

5. The logarithm of the average temporal FFT PSDs from pre- and poststimulus neocortical EEG segments, when plotted against log frequency, revealed $1/f$ -type spectra in both pre- and poststimulus segments for negative/aversive conditioned stimuli (CS-) and positive/rewarding conditioned stimuli (CS+). The α' - and β' -coefficients from the regression of Eq. 2 onto the average PSDs were significantly different between pre- and poststimulus segments, owing to the evoked potentials, but not between CS- and CS+ stimulus segments.

6. Spatiotemporal patterns were invariant over all frequency bins in the $1/f$ domain (20–100 Hz). Spatiotemporal patterns in the 2- to 20-Hz domain progressively differed from the invariant patterns with decreasing frequency.

7. In the spatial frequency domain, the logarithm of the average spatial FFT power spectra from pre- and poststimulus neocortical EEG segments, when plotted against the log spatial frequency, fell monotonically from the maximum at the lowest spatial frequency, downwardly curving to a linear $1/f$ spectral domain. This curve in the $1/f$ spectral domain extended from 0.133 to 0.880 cycles/mm in the PPC and from 0.095 to 0.624 cycles/mm in the neocortices.

8. Methods of FFT and principal component analysis (PCA) EEG decomposition were used to extract the broad-spectrum waveform common to all 64 EEGs from an array. AM patterns for the FFT and PCA components were derived by regression. They were shown by cross-correlation to yield spatial patterns that were equivalent to each other and to AM patterns from calculation of the 64 root-mean-square amplitudes of the segments.

9. Each spatial AM pattern was expressed by a 1×64 column vector and a point in 64-space. Similar patterns formed clusters, and dissimilar patterns gave multiple clusters. A statistical test was

devised to evaluate dissimilarity by a Euclidean distance metric in 64-space.

10. Significant spatial pattern classification of CS- versus CS+ trials (below the 1% confidence limit for 20 of each) was found in discrete temporal segments of poststimulus data after digital temporal and spatial filter optimization.

11. Varying the analysis window duration from 10 to 500 ms yielded a window length of 120 ms as optimal for pattern classification. A 120-ms window was subsequently stepped across each record in overlapping intervals of 20 ms. Windows in which episodic, significant CS+/CS- differences occurred lasted 50–200 ms and were separated by 100–200 ms in the poststimulus period.

12. Neocortical spatial patterns changed under reinforcement contingency reversal, showing a lack of invariance in respect to stimuli and a dependence on context and learning, as previously found for the olfactory bulb and PPC.

13. The EEG data contributing to classification were homogeneously distributed across wide temporal and spatial spectral bands and across the spatial array of electrodes. Patterns could be resolved with as few as 16 channels. No channel was more or less contributory to classification than any other.

14. The aperiodic waveforms, the rapid global state changes, the context dependence of the AM patterns, and the homogeneous distribution of neural activity suggest that the neural events formed during perception are constructed by cooperative population dynamics in both paleocortex and neocortex. These characteristics so far provide the most powerful evidence for spatially coherent, aperiodic oscillations manifesting macroscopic cortical states that are spatially continuous over areas >5 mm diam and that last <200 ms.

INTRODUCTION

Correlation of spatial patterns of neural activity in the olfactory receptor layer and olfactory bulb with classes of odors was first postulated by Adrian (1950). Subsequent studies of the spatial patterns of activity among receptors (Moulton 1976) and periglomerular cells with 2-deoxyglucose (Lancet et al. 1982) or optical dye recording (Kauer 1987), and of the requisite degree of topographic mapping in the primary olfactory nerve between them (Freeman 1974), have supported this hypothesis of sensory coding. However, unit studies of mitral cells have thus far failed to yield an unequivocal central neurosensory code for odors (Thommeson 1978; Wells et al. 1989).

Studies of electroencephalograms (EEGs) in the olfactory bulb revealed close statistical correlations in both time, space, and EEG amplitude with nearby single- and multiple-unit activity (Eeckman and Freeman 1990, 1991; Freeman 1975). Large numbers of neurons were active in response

to odorant stimuli, so that the failure of a spatial sensory code to previously emerge was possibly due to inadequate sampling by microelectrode recording. On the premise that dendritic potentials gave access to neuron population activity, spatial analysis of EEG patterns from arrays of 64 epidural electrodes was undertaken. Evidence was sought for spatial coding at a macroscopic or neural population level. Within training experiments, spatial patterns were found in respect to odors that rabbits had learned to discriminate (Freeman and Viana Di Prisco 1986). The patterns took the form of amplitude modulation (AM) of a spatially coherent oscillation in the gamma frequency (20–80 Hz) range (Bressler and Freeman 1980).

However, the spatial patterns lacked invariance with respect to odorant conditioned stimuli, showing instead a dependence on brain state, behavioral context, and training history (Freeman 1991c). This context dependence referred to the meaning of the odors for the subjects, including both positive (i.e., food or drink reward) and negative (i.e., a mild shock or other aversive stimuli) reinforcement. The patterns did not reflect a strictly sensory code. A nonlinear dynamic model was constructed to show how a chaotic carrier wave could be generated (Freeman 1987), and how it might be modulated to give context-dependent spatial patterns in response to learned input (Yao and Freeman 1990).

The aim of the present report is to extend the approach of multichannel surface EEG recording and analysis to the visual, auditory, and somatic neocortices. Analyses of neocortical recordings from multiple electrodes on the human scalp (Barlow 1993; Livanov 1977; Walter 1953) and from arrays placed onto the exposed cortex [25 channels by Lilly (1949, 1954); up to 100 channels by Livanov (1977); and 400 channels by DeMott (1966)] showed the existence of complex patterns of aperiodic activity (Mickle and Ades 1954). DeMott (1966) concluded that sensory input "is presented to the cortex not as a map, but as a very complex spatial-temporal sequence, in which every part of the cortex participates in displaying information from every part of the [sensory] field" (p. 29). Those efforts failed to yield a theory of sensory or perceptual coding. Previous results from the study of olfaction (Freeman 1987) suggested that the failure was due to inadequate sampling of EEG data from trained animals. Here we report on the analysis of a massive data base of ≥ 50 Gbytes, representing an iterative analysis of 2 yr of 64-channel EEG recordings from 14 subjects and four cortical areas, enabled by recent developments in high-speed computing. The results show that the fundamental characteristics of EEGs from the three sensory neocortices resemble olfactory EEGs in displaying spatial AM patterns of a spatially coherent, aperiodic carrier wave, which serve to classify EEG segments with respect to discriminated sensory stimuli. These AM patterns reflect the context and history of training, not merely stimulus coding and classification.

METHODS

Animal preparation

Square arrays of 64 (8×8) 0.25-mm-diam stainless steel, epoxy-insulated wire electrodes were prefabricated with connectors (Eastman 1975) before surgery. Interelectrode distances for paleocortical and neocortical arrays were 0.56 and 0.79 mm, respec-

FIG. 1. Schematic of electrode array implant sites. Each array was chronically implanted onto the epidural surface of the left cortical hemisphere of the New Zealand White rabbit. This figure represents the left, lateral surface of the cortex and demarcates the general location of each array placement. Note that the olfactory bulb (OB) implant was located on the dorsal aspect of the bulb and has been included in this schematic as a reference to previous work. PPC, prepyriform cortex; SOM, somatosensory cortex; AUD, auditory cortex; VIS, visual cortex.

tively. To make the array as large as possible without spatial aliasing, the maximum allowable interelectrode spacing was found that provided the optimal spatial sampling frequency as determined by spatial spectral analysis (Freeman and Baird 1987).

Each of 14 female New Zealand White rabbits (2.5–4.5 kg) was chronically implanted with an epidural array on the prepyriform cortex (PPC), the visual cortex (Hollander and Halbig 1980; Hughes and Vaney 1982; Thompson et al. 1950), the auditory cortex (Galli et al. 1971; McMullen and Glaser 1982), or the somatic cortex (Gould 1986). There were four PPC, two visual, five auditory, and three somatic implants; all of the arrays were placed onto the left cortical hemisphere (Fig. 1). During array implantation a full surgical plane of anesthesia (4% isoflurane-O₂ mixture) was maintained via endotracheal intubation; standard aseptic techniques were observed. After rectangular trephination, an array was placed directly onto the intact dura. K-Y jelly was applied to protect exposed dura at the margins of the array, and the opening was sealed with acrylic cement used to fix the array to the calvarium. Structural ground and reference screws were inserted at six sites into the skull (2 anterolateral to the coronal suture, 2 on the medial aspect of the supraorbital ridge, and 2 1.0 cm posterolateral to the bregma). Drying and infection of the exposed soft tissues and corneas was prevented with periodic application of 5% baytril-saline solution. Buprenorphine (0.00875 mg/kg sc) was postoperatively administered. All procedures were conducted according to protocol approved by the University of California at Berkeley Animal Care and Use Committee with veterinary supervision by the Office of Laboratory Animal Care.

POST MORTEM ANIMAL DISPOSITION. After all experiments were complete, each animal was killed by pentobarbital sodium overdose (120 mg/kg Nembutal iv). Each rabbit was perfused with 10% Formalin and an autopsy was performed to verify placement of the electrode array, to check for damage of the underlying cortical tissue, and to check for regrowth of bone over the cortical window.

Recording

The EEG was recorded monopolarly with respect to that cranial reference electrode nearest the array and amplified by fixed-gain (10K) ISO 4/8 differential amplifiers (World Precision Instruments). Each channel was filtered with single-pole, first-order analog resistance/capacitance (RC) filters (6 dB/octave falloff) set at 100 Hz (3 dB point) and 0.1 Hz. Records of 64 12-bit samples multiplexed at 10 μ s were recorded at a 2-ms digitizing interval

(500 Hz) for 6 s and stored as signed 16-bit integers. The incremental time delay caused by multiplexing of the EEG was corrected off-line. Bad channels associated with movement artifact or electromyogram were identified by visual editing and replaced off-line by averaging the signals of two vertically or horizontally adjacent channels. For each experiment there were no more than 10 bad channels.

Conditioning

After 1 wk for postoperative recovery each rabbit was familiarized with the experimental setup (Viana Di Prisco and Freeman 1985) while placed in a restraining box to decrease movement artifact in the EEG recordings. A pneumograph belt was attached around the chest for a digital record of respiration; surgical clips were placed onto the posterolateral aspect of the left cheek for unconditioned stimulus delivery; and the restrained animal was placed into an electrically shielded chamber with adequate ventilation and a source of white noise at 72 dB. The PPC rabbits were fitted with a nose cone for odor delivery and the auditory rabbits were fitted with earphones for delivery of auditory stimuli. Each rabbit was given a stimulus modality specific to the cortical area of implantation (e.g., rabbits implanted with arrays over the visual cortical areas received visual stimuli, etc.). The EEG was analyzed for movement artifacts and for the presence of stimulus-specific activity, including oscillations in the PPC and evoked potentials in the neocortical sites, to confirm usable EEG recordings.

After familiarization there was one basic experimental paradigm. Each rabbit was classically conditioned to discriminate between two different modality-specific stimuli. Each stimulus was delivered on 20 trials randomly sequenced in intertrial interval and stimulus order, thereby yielding a 40-record experiment. The 6-s recording period was divided into 3 s of prestimulus EEG recording and 3 s of poststimulus EEG with the stimulus arriving at 3,000 ms (3,500 ms for olfactory stimuli). During the recording experiment the rabbit was trained to discriminate between an unreinforced stimulus (CS-) and a reinforced stimulus (CS+) paired to a mild electric shock (unconditioned stimulus), which had sufficient intensity to elicit a skin twitch (unconditioned response). The unconditioned stimulus was delivered via a pair of skin clips placed superficially at the base of the left ear or onto the posterolateral aspect of the left cheek. The unconditioned stimulus arrived at the end of the 6-s trial period and consisted of four to five electrical pulses (1–5 mA) delivered in a window of 10 ms. Previous work (Davis and Freeman 1982) demonstrated acquisition of a conditioned response (CR) during training to reinforced olfactory stimuli within three to four trials. Presence of a CR was measured as a change in the poststimulus respiration (Freeman et al. 1983). This basic paradigm was replicated once during the 2nd and 3rd wk. The CS-/CS+ contingencies were reversed during the 3rd wk with the same animal; the CS+ that was initially paired with the unconditioned stimulus became the CS- and vice versa. Each rabbit was trained to the basic paradigm once per week for a total of three experiments per animal at the conclusion of this project. In the case of the PPC and auditory implants, one of each animal did not survive through the last experiment.

Stimuli

Four pairs of discriminable stimuli were used throughout these experiments. Olfactory stimuli typically included food flavorings (e.g., peppermint and coconut extracts) delivered by an olfactometer that injected each test odor into a constant stream of charcoal-filtered air flowing into a mask attached over the rabbit's muzzle (Freeman and Schneider 1982). Arrival time of each odor occurred at 3,500 ms (the measured time lag through the olfactometer). Odorants were removed from the mask by a mild vacuum sufficient

to prevent the spread of the odorants into the recording chamber. Duration of the olfactory stimuli was 2.5 s.

Visual stimuli consisted of two full-field flashes varying only in intensity lumens (3.6 vs. 2.8 ft.-cd). During presentation of visual stimuli each animal was placed into a dark chamber with no background light. Duration of the visual stimuli was 10 ms. Auditory stimuli consisted of two amplitude-invariant sinusoids differing only in frequency (500 vs. 5,000 Hz), delivered binaurally via a pair of Sony MX-2 stereo earphones at 72–84 dB above 72 dB white noise within the recording chamber. Duration of auditory stimuli was 100 ms. Somatic stimuli consisted of an air puff onto the contralateral (to the implant site) cheek or onto the contralateral hindquarters. Duration of somatic stimuli was 3.0 s.

Data analysis

AVERAGES OF EEG SEGMENTS. Display of paleocortical and neocortical EEGs was by the spatial ensemble average (SEA) and standard deviation (SD) from single trials across 64 channels. Temporal ensemble averages (TEAs) were computed from SEAs across 40 experimental trials (20 CS-/CS+) to give the average evoked potential and its SD for each experiment. Temporal spectra of the EEGs were calculated by applying the fast Fourier transform (FFT) (Press et al. 1988) to contiguous 500-ms pre- and poststimulus segments of SEAs. Each time series was padded with zeros until the number of points reached a power of 2, and each time series was smoothed with a Hamming window before FFT decomposition. Power spectral densities (PSDs) derived from the FFT were averaged across the 20 CS- and 20 CS+ records for each time window, thereby yielding the average PSD and corresponding standard error (SE) for all frequencies below the 100-Hz low-pass analog filter cutoff. To test how much the average PSD deviated from a $1/f$ -type spectra in the gamma range, a line described by Eq. 1 was linearly regressed onto the log-log PSD plot in the 20- to 80-Hz range

$$\log_{10} P = \alpha - \beta \log_{10} f \quad (1)$$

Eq. 1 can be rewritten as

$$P_k(f) = 10^{\alpha'/k} / f^{\beta'} \quad \forall k \in \{1, 2, \dots, 64\} \quad (2)$$

where P is the PSD of each channel (k) at every frequency (f); α is the Y -intercept of the PSD regression line, and β is the slope of the regression line from Eq. 1. Because regression of a line onto the log-log frequency spectra naturally biases the high-frequency portion of the average log-log PSD, a curve described by Eq. 2 was regressed onto the temporal spectra. Calculation of the nonlinear coefficients, α' and β' , was determined by the use of α and $-\beta$, respectively, as initial guesses for the Levenberg-Marquardt method of nonlinear regression (Press et al. 1988) of Eq. 2 onto the average 20- to 80-Hz PSD. The average PSD $\pm$ SE expressed to the 95% confidence level was plotted against the curve described in Eq. 2. Regression onto the 20- to 80-Hz domain of the neocortical PSD as opposed to the 20- to 100-Hz domain was chosen because these frequencies were minimally affected by the 100-Hz RC filter. Deviations from $1/f$ spectra were indicated by those areas of the regression curve lying outside of the SE curves. Similar regression analyses for the PPC data sets were conducted with the use of the 10- to 50-Hz portion of the frequency spectra. This frequency range was expected to reveal excess power in the 50- to 80-Hz band, which could force a poor fit of Eq. 2 to the PPC PSD.

DERIVATION OF SPATIOTEMPORAL PATTERN FROM 64 TRACES. Spatial patterns of EEG activity were calculated by decomposing or representing EEG time segments of specified length from the 64-channel recordings. Four methods were used to derive spatial patterns: FFT (Press et al. 1988) and modified FFT decomposition

(Freeman 1987; Freeman and Viana Di Prisco 1986); principal component analysis (PCA) (Freeman and Van Dijk 1987; Maier et al. 1987); and root-mean-square (RMS) (Freeman 1978) computation of amplitude activity. FFT decomposition yielded the spatiotemporal pattern of PSD activity at a certain frequency. The modified FFT returned the PSD at the dominant frequency varied by linear amplitude and frequency modulation across the EEG segment. Modified FFT and PCA algorithms yielded the waveform common to all 64 channels. Use of the RMS was justified by the small value of the residuals, after removal of the dominant component by PCA. The spatial pattern of each common waveform was expressed by the 8×8 PSD matrix of the largest modified FFT component, the 8×8 matrix of the factor loadings of the dominant factor of PCA, or the 8×8 matrix of RMS amplitudes. Each matrix was represented as a 1×64 column vector $\bar{V}$

$$\bar{V} = R_k \quad \forall k \in \{1, 2, \dots, 64\} \quad (3)$$

where R is the spatial pattern matrix for each channel (k). The degree of conformance between the modified FFT, PCA, and RMS analysis techniques was measured by calculating the nonparametric correlation coefficients (r) between sets of patterns. Each correlation coefficient was normalized to a z score before averaging and retransformed to its r value with its asymmetric SDs.

RELATING SPATIOTEMPORAL PATTERN TO TEMPORAL FREQUENCY SPECTRUM. To determine whether the spatiotemporal patterns of EEG PSDs differed across the temporal frequency spectra, 128- and 256-ms pre- and poststimulus windows of experimental EEG data taken from 20 CS- and 20 CS+ records were transformed into 1×64 vectors with the RMS and FFT algorithms. The normalized RMS pattern was employed as a reference pattern. The Euclidean distance from the reference pattern to each pattern reconstructed from the normalized PSD from the first frequency (2 Hz) of the FFT decomposition was calculated and averaged across 40 records. This process was repeated for each normalized PSD bin, thereby yielding a pre- and poststimulus frequency spectrum of distances from the reference pattern to each frequency pattern

$$D_f(\bar{V}', \bar{V}^{(f)}) = \sqrt{\sum_{k=1}^{64} (V'_k - V_k^{(f)})^2} \quad \forall f \in \{2, 4, \dots, \tilde{n}\} \quad (4)$$

where $\bar{V}'$ is the 1×64 RMS reference vector; $\bar{V}^{(f)}$ is the 1×64 FFT PSD vector for each frequency bin (f) ranging from 2 Hz to the last frequency bin ($\tilde{n}$) under 100 Hz; and D_f is the Euclidean distance from the reference pattern to the FFT PSD pattern reconstructed at each frequency bin.

SPATIAL PATTERN CLASSIFICATION. The search for significantly different, stimulus-induced, spatial CS-/CS+ patterns was conducted by stepping a T -ms window along individual records at overlapping 20-ms time intervals, where T was varied from 10 to 500 ms in search of an optimal value for classification. Each window, having 64 EEG traces, yielded a 1×64 column vector in amplitude $\bar{V}$

$$\bar{V}^{(i,j)} = (R_k^{(i,j)}) \quad \forall k \in \{1, 2, \dots, 64\}, \quad j \in \{1, 2, \dots, n\}, \quad i \in \{1, 2, \dots, 40\} \quad (5)$$

where $\bar{V}^{(i,j)}$ is the 1×64 spatial pattern vector at time window (j), record (i); n is the number of time windows, and R is the component amplitude for each channel (k). This analysis yielded 20 CS- patterns and 20 CS+ patterns for each time step. These patterns were further divided into two subgroups of 10 CS- patterns and two subgroups of 10 CS+ patterns. Each pattern defined a point in 64-space and was normalized to zero mean and unit SD

to remove stimulus-specific amplitude differences between patterns. For each step (j) in a subgroup (m) a series of centroids $\bar{C}^{(m,j)}$ was calculated in 64-space

$$\bar{C}^{(m,j)} = 1/10 \sum_{i=10(m-1)+1}^{10m} \bar{V}^{(i,j)} \quad \forall m \in \{1, 2, 3, 4\}, \quad j \in \{1, 2, \dots, n\} \quad (6)$$

where $m = 1, 3$ represents the CS- centroids, and $m = 2, 4$ represents the CS+ centroids for each time window. Classification of patterns as CS- or CS+ was determined by calculating the Euclidean distances of all patterns in subgroups 1, 2 to centroids 3, 4 within each of n windows

$$D(\bar{C}^{(m,j)}, \bar{V}^{(i,j)}) = \sqrt{\sum_{k=1}^{64} (C_k^{(m,j)} - V_k^{(i,j)})^2} \quad (7)$$

This process was repeated by cross-classifying all patterns in subgroups 3, 4 by centroids 1, 2. A spatial pattern in a test subgroup was classified correctly if the distance between that pattern and the centroid of its training subgroup was less than the distance between the same pattern and the centroid of the opposite training subgroup

$$D(\bar{C}^{(2\tilde{m}-1,j)}, \bar{R}^{(i,j)}) < D(\bar{C}^{(2\tilde{m},j)}, \bar{R}^{(i,j)}) \quad \forall \tilde{m} \in \{1, 2\}, \quad i \in \{20(2 - \tilde{m}) + 1, \dots, 20(3 - \tilde{m})\} \quad (8)$$

where $\tilde{m} = 1$ represents centroids 1, 2 and indexes i to patterns 21–40; and where $\tilde{m} = 2$ represents centroids 3, 4 and indexes i to patterns 1–20. What emerged was a temporal sequence of ratios ($x:40$) where x is the number of correctly discriminated spatial patterns within each window (j). The probability (p) that the number of patterns that were correctly cross-classified was significant was determined with a cumulative binomial probability distribution scale

$$p_j = \sum_{r=x}^q [q!/r!(q-r)!] \bar{p}^r (1-\bar{p})^{q-r} \quad \forall j \in \{1, 2, \dots, n\} \quad (9)$$

where q is the number of trials (40) (Barrie and Freeman 1994; Press et al. 1988). Because the calculation of Eq. 9 assumed that there was an equal probability that any spatial pattern could be classified as a CS- pattern or as a CS+ pattern, $\bar{p} = 0.5$. This calculation was repeated for each time window giving n probability values in a time series; p_j , where $j = 1, \dots, n$. The average change for probability values across a series of analysis windows was defined as

$$\overline{\Delta p} = 1/(n-1) \sum_{j=2}^n |\log_{10}(p_j) - \log_{10}(p_{j-1})| \quad (10)$$

ONE- AND TWO-DIMENSIONAL TEMPORAL AND SPATIAL DIGITAL FILTERING. Previous work demonstrated significantly improved classification of paleocortical EEG spatiotemporal patterns after temporal (Freeman and Viana Di Prisco 1986) and spatial (Freeman and Baird 1987) digital filtering. Optimizing temporal filters involved searching a set of band-pass filter parameter spaces in order to maximize the number of correctly classified poststimulus patterns while minimizing the number of falsely classified prestimulus patterns. This band-pass temporal filter space was defined by a variable low-cut setting beginning at 5 Hz and stepped every 5 Hz until the constant high-cut setting of 100 Hz (the high-cut analog filter setting defining the usable experimental frequency space) was reached. For each band-pass filter setting the experimental data was digitally one-dimensionally filtered, transformed into a series of RMS spatial patterns, normalized, and reclassified. This analysis yielded a band-pass temporal filter tuning curve for each individual data set. From the tuning curve an optimal band-

pass temporal filter setting was employed throughout the remainder of the analysis of that data set.

Spatial spectral analysis of the 8×8 RMS amplitude matrix from a 120-ms segment of EEG was performed by imbedding it in a 32×32 matrix of zeros, translating the data to bring the zero spatial frequency values to the center of the 2D plot of power, and applying a 2D FFT (Freeman and Baird 1987; Press et al. 1988). Spatial PSDs derived from the 2D FFT were radially integrated in order to obtain the PSD in cycles per millimeter

$$S_i = 1/c \sum_{h=0}^{\nu_i'} \sum_{v=0}^{\nu_i'} P'_{h,v}$$

where

$$D'_{i-1} \leq \sqrt{h^2 + v^2} \leq D'_i \quad \forall i \in \{1, 2, \dots, 15\} \quad (11)$$

where P' is the 2D PSD; h is the horizontal distance of P' from the center of the array; v is the vertical distance of P' from the center of the array; D' is the radius (in mm) of a concentric circle mapped onto the 32×32 matrix; i is the index of one concentric circle (15 were mapped onto the matrix of PSDs); c is the number of PSDs satisfying the condition $D'_{i-1} \leq \sqrt{h^2 + v^2} \leq D'_i$; and S is the average 2D PSD for those values within a circle containing the center four electrodes for the first integration or an annulus containing four to six electrodes for subsequent integrations. Radially integrated spatial PSDs were subsequently averaged across the 20 CS- and 20 CS+ records for contiguous pre- and poststimulus portions of an experiment analyzed with the RMS algorithm, thereby yielding the average spatial PSD in cycles per millimeter and mean $\pm$ SE expressed to the 95% confidence level. Curves were regressed onto the average 2D PSD with the use of Eq. 2 for only the high-frequency portion of the PSD defined as that above 0.09 cycles/mm and that below the spatial Nyquist frequency (0.9 cycles/mm for the PPC 2D FFT and 0.62 cycles/mm for the neocortical 2D FFT).

Spatial filters were optimized (after the data set had been filtered at an optimal band-pass temporal filter setting) by imbedding the 8×8 RMS amplitude matrix in a 32×32 matrix of zeros, translating the data, calculating the 2D FFT, and applying an exponential band-pass digital spatial filter defined by a variable low-cut setting beginning at the minimal resolution of the 2D FFT and stepped at every subsequent resolvable spatial frequency until the constant high-cut setting was reached. The constant high-cut setting was defined as that immediately below the spatial frequency artifact (the spatial Nyquist frequency) induced by the interelectrode spacing of the array (Freeman and Baird 1987). The subsequent 32×32 matrix of 2D FFT values was inverse transformed back into an 8×8 matrix of spatially filtered RMS values. Optimization of spatial filters involved searching the band-pass spatial filter parameter space in order to maximize the number of correctly classified poststimulus patterns while minimizing the number of falsely classified prestimulus patterns. This analysis yielded a band-pass spatial filter tuning curve for each individual data set. Each data set was ultimately classified with the use of an optimized temporal and spatial filter setting.

QUANTIFYING THE SPATIAL EEG DISTRIBUTION OF NEURAL ACTIVITY ACROSS CHANNELS. The contribution in EEG activity from any electrode as part of a subset of electrodes from the 64-channel array was assayed by repeating the cross-classification measure after groups (0, 2, 4, 8, 16, 24, 32, 48, 56, 63) of randomly selected channels were deleted. Groups of random channels were selected by a multiplicative congruential random-number generator with a period of 2^{32} . This analysis was iterated 50 times for each group of deleted channels. The average number of patterns classifying below chance levels ($P < 0.50$) across analysis windows was calculated for each group. SEs were expressed to the 99% confi-

dence level. The distribution of neural activity across the array was assayed by keeping a running total of how many times each channel was deleted across groups, and how many cases classified correctly when that channel (as a subset of other randomly deleted channels) was absent. This yielded an average number of spatial patterns that classified correctly as a function of individual channel deletion. The following questions were asked: which channels (if any) were more or less important than average for classification, and how did the goodness of classification decline with the number of channels deleted?

RESULTS

Temporal analysis

Inspection of raw EEGs from the PPC conformed to previous results (Bressler 1987; Freeman and Schneider 1982). An SEA of the PPC recordings across the 64-channel array retained the series of high-frequency bursts separated by broadband interbursts all riding on a low-frequency wave highly correlated with the respiration (Fig. 2, *top trace*). The same procedures applied to the neocortical data sets yielded the SEA time series with no bursts but with an evoked potential marking the arrival at the sensory cortex of the afferent volley of action potentials relayed through the thalamus (Chang 1959) from the periphery (Fig. 2, *bottom 3 traces*). The low-SD time series for each SEA indicated high spatial coherence across the neocortical arrays. When the raw PPC EEG recording from a single channel was plotted against the respiratory wave, each olfactory burst began one quarter cycle into the inspiratory phase and lasted on the order of 80–200 ms (Fig. 3, *top*). Raw neocortical EEG recordings plotted against the respiratory wave showed no such correlation (Fig. 3, *bottom*), indicating that respiratory activity was not a forcing function for neocortical events.

Averaged 20-CS- and 20-CS+ SEAs from a single experiment yielded the TEA, including the average evoked potential. The PPC TEA showed that temporal averaging of olfactory EEGs blurred burst patterns, because oscillations within bursts were not phase-locked to the onset of the olfactory stimulus (Fig. 4, *top trace*). Neocortical TEAs revealed activity time-locked to the stimulus arrival. Background EEG activity was smoothed, increasing the signal-to-noise ratio of the evoked potential above the neocortical SEAs (Fig. 4, *bottom 3 traces*). Within all four sensory modalities the SDs for the TEAs were greater than the SDs from the SEAs because of high variance in spatial EEG pattern over trials.

Temporal spectra were used to locate peaks, particularly in the gamma band (Bressler 1984, 1987; Bressler et al. 1980, 1993; Engel et al. 1992; Freeman 1991b; Freeman and Barrie 1994; Gray 1994; Gray et al. 1989; Koch 1993). Averaged spectra from 500-ms windows of poststimulus (3,000–3,500 ms) EEGs were computed over 40 records from the PPC and visual, somatic, and auditory cortices and plotted against log frequency. Power spectra were calculated from the SEA, because the average PSD across each of the 64 channels was statistically indistinguishable from the PSD of the SEA. Curves described by Eq. 2 were regressed onto the 10- to 50-Hz frequency range for the PPC data and onto the 20- to 80-Hz frequency range for the neocortical data and plotted against each average PSD and mean $\pm$ SE (95%

FIG. 2. Examples of spatial ensemble averages (SEAs) (—) and standard deviations ($\cdots$) from 4 cortical areas, calculated by averaging 64 electroencephalograms (EEGs) simultaneously recorded during 1 experimental trial. In all recordings the stimulus was initiated at $t = 3,000$ ms. In the case of olfactory stimuli there was a 500-ms delay, so that the odor arrived at the rabbit's nose cone at approximately $t = 3,500$ ms.

confidence level). Because of an expected excess of power in the 50- to 80-Hz domain (the range for olfactory bursting), regression onto the PPC PSD utilized only those frequencies in the most linear portion of the PSD (10–50 Hz). The criterion was adopted that a spectrum was $1/f$ if its regression curve lay completely within the SEs. Deviant peaks in the gamma frequency range were sought, because gamma activity has been proposed as a vehicle for feature binding (Eckhorn et al. 1992; Engel et al. 1992; Freeman

1991a; Gray et al. 1989). The PPC spectra closely matched previous results (Boudreau and Freeman 1963; Bressler 1987; Freeman 1975) with peaks in PSDs at frequencies between 50 and 80 Hz (Fig. 5, *top*). Neocortical results (Fig. 5, *bottom 3*) illustrated that there were no statistically significant spectral deviations within the gamma frequency range for the neocortical EEG. Occasional deviations from $1/f$ within the gamma range were not reproducible across other neocortical data sets. The 80- to 100-Hz PSD segment

FIG. 3. Respiration, as measured with a pneumograph (· · ·), and EEGs (—) were correlated in the prepyriform cortex (PPC) (*top*) but not in the visual cortex (*bottom*).

of the regression curve for the neocortical recordings lay above the SE curves, indicating that EEG activity was attenuated by the low-pass analog RC filter.

Differences between the pre- and poststimulus PSD across all cortical areas were sought by calculating the average, normalized α' -coefficients and β' -coefficients from the regression of Eq. 2 onto the average CS- /CS+ PSD within the 20- to 80-Hz range for the neocortical data sets. The average α' - and β' -coefficients were plotted with the corresponding mean $\pm$ SE (95% confidence level) for the visual and somatic cortices (Fig. 6). For all neocortical recordings, the average, normalized α' - and β' -coefficients of the average PSD defined baseline prestimulus levels. After stimulus onset and within the first 128-ms poststimulus period, the α' coefficient for the gamma band visual cortical recordings increased for ~ 750 ms. Somatic and auditory records showed an immediate poststimulus increase in α' for the gamma band, and a subsequent and sustained decrease in α' for the duration of the poststimulus period (Fig. 6). Every change in α' was associated with an inverse change in the steepness of slope for the $1/f$ band PSD, as indicated by β' . The values for pre- and poststimulus α' - and β' -coefficients for the average CS- and CS+ PSDs lay within the SE curves, indicating that spectra between the discriminanda did not differ. These findings held for all sensory cortices and animals. The importance of changes in the gamma band α' - and β' -coefficients could reflect changes in the fractal dimension of the dynamics of the EEG generated from the neocortex (Higuchi 1990).

Spatiotemporal pattern representation

To determine the spatial amplitude pattern of the common waveform, each 64-channel segment of EEG data (Fig. 7, *left*) was transformed into a spatial pattern (Fig. 7, *right*)

by the methods of FFT, modified FFT, PCA, and RMS. With the modified Fourier method a sum of five cosines was fit to the data (Freeman and Viana Di Prisco 1986). The dominant frequency component comprised, on average, 60–70% of the EEG variance. Components 2–5 had the same spatial pattern as the dominant component. It also gave the spatial pattern of phase for each frequency; its use is discussed elsewhere (Freeman 1991a; Freeman and Baird 1987) and was previously thought to be the ideal method for resolving EEG spatial patterns. This method is computationally intensive, and it does not work well with EEG segments with a $1/f$ spectra instead of narrowband bursts, but its use was included with this analysis to quantitatively contrast modified FFT spatiotemporal patterns resolved in the neocortex with other methods of EEG spatial pattern resolution utilized throughout the remainder of this study. The first PCA component represented 90–99% of the EEG variance. Its factor loadings defined the spatial pattern or mode. Figure 8 (*top*) illustrates representative modified FFT and PCA decompositions for the average waveform from Fig. 7 (*left*). Because the first PCA component comprised most of the variance, closely approximating the raw EEG (Fig. 8, *bottom*), an RMS calculation was more desirable in terms of computational time. Table 1A compares the modified FFT and PCA methods of neocortical EEG decomposition with the RMS algorithm by calculating the average, normalized nonparametric correlation coefficient between 9,000 neocortical spatial patterns. Table 1B shows the same comparison for a PPC EEG experiment. If the nonparametric correlation coefficient indicated a match between two spatial patterns and if the probability of that match was <0.001 , then the criterion that those two spatial patterns were identical was satisfied. Because the RMS method yielded spatial patterns significantly correlated with both the modified FFT and PCA spatial modes, the RMS method was employed throughout the remainder of this study of spatial patterns.

FIG. 4. Temporal ensemble averages (TEAs) (—) and standard deviations ($\cdot \cdot \cdot$) were calculated for the PPC and visual, somatic, and auditory cortices by averaging the SEAs of 40 records from 1 experiment. Temporal averaging of the PPC SEAs blurred the pattern of olfactory bursts, as shown in Fig. 3 (*top traces*). Temporal averaging of the neocortical SEAs revealed that there was EEG activity time-locked to the arrival of the stimulus as demonstrated by the increased signal-to-noise ratio of the evoked potential above the neocortical SEAs and by the smoothing of the control period TEA. There was no analogous time-locked PPC TEA activity.

Conformance of neocortical spectra to Eq. 2 implied that the 1×64 FFT PSD spatiotemporal pattern vector was defined at every frequency bin by the 64 α' -coefficients of the regression curve onto each channels PSD and that the same pattern was only rescaled across frequency bins by f^β . Therefore each pattern could not significantly vary given a constant PSD β' -coefficient for all 64 channels. Curves independently regressed onto the gamma frequency (20–80

Hz) domain of the PSD, from each of the 64 channels, had the same β' within 95% confidence limits but differed in α' . This meant that each spatiotemporal pattern was equivalent within the 20- to 80-Hz range, but that there might be other spatial patterns in the low (2–20 Hz) or high (80–100 Hz) frequency range. To test every pattern at every frequency <100 Hz within a 128-ms pre- and poststimulus time frame, the Euclidean distance from a normalized RMS reference

FIG. 5. Average temporal power spectral densities (PSDs, —) and $\pm 95\%$ confidence intervals ($\cdots$) were calculated from the prepyriform, visual, somatic, and auditory EEGs. Each PSD was averaged across 40 records from a Hamming smoothed, 500-ms poststimulus EEG window. Regression curves calculated by the use of Eq. 2 were fit to the 10- to 50-Hz domain of the PPC PSD and the 20- to 80-Hz gamma domain of the neocortical PSDs.

pattern to every reconstructed, normalized FFT PSD bin spatiotemporal pattern was calculated and averaged across 20 CS- and 20 CS+ records (Fig. 6 reviews the dynamic changes in α' for pre- and poststimulus segments). Average Euclidean distances from RMS to FFT PSD patterns (means $\pm$ SE) (99% confidence limits) are shown for the visual and somatic cortices in Fig. 9. There were found to be two domains of spatiotemporal patterns: the low-frequency range (2–20 Hz), and the $1/f$ range. The spatiotemporal patterns within the $1/f$ range did not statistically differ, but those within the low-frequency range differed progressively with decreasing temporal frequency. No distinctive spatial patterns emerged within the 2- to 20-Hz domain. The centroid of the points was near the centroid for the $1/f$ cluster, but the points were widely scattered, mostly outside of the cluster. These results were replicated for the auditory cortex, and for all three neocortices with FFT decomposition windows 256 ms in length. Those FFT PSD spatiotemporal patterns within the $1/f$ domain conformed to the EEG spatial patterns resolved by the modified FFT, PCA, and RMS algorithms.

Spatial pattern classification

Segmentation of EEGs from the olfactory system was facilitated by the presence of EEG gamma bursts recurring at the respiratory rhythm. EEGs from the neocortices showed no alpha, theta, or gamma bursts and no correlation between the EEG and the respiratory rhythm. The average evoked potential marked the arrival of the afferent volleys but failed to demarcate significant segments of poststimulus EEGs. Therefore successive EEG patterns were extracted by moving a fixed-length analysis window across each set of 40 records (comprising 1 experiment) in overlapping steps. Given the overlapped set of spatial patterns, a method of cross-classification was used to classify patterns as closer to a CS- centroid or closer to a CS+ centroid by a Euclidean distance metric. Each 40-record experiment was transformed into 40×225 (the number of analysis windows) spatial patterns. A testing of this method for false pattern classification was accomplished by generating 40×225 random (flat distribution) patterns, normalizing each pattern to zero mean and unit SD, and performing a classification analysis across

FIG. 6. α' -Coefficients (left) and β' -coefficients (right) were calculated by regression of Eq. 2 onto the 20- to 80-Hz band of the PSD, averaged across 40 negative/aversive conditioned stimulus (CS-) – positive/rewarding conditioned stimulus (CS+) EEG records from each experiment. The average PSDs from individual experiments were normalized and averaged across visual ($n = 6$) and somatosensory ($n = 8$) experiments. Coefficients from the auditory EEGs conformed to the pattern for somatic cortex.

the entire set. Among the 225 time frames of random patterns, only 1 frame had a number of patterns classifying below the 1% significance level.

A salient feature by which two similar groups of spatial patterns can be classified with a Euclidean distance metric was the pattern of global amplitude activity. Because this study concerns differences in pattern of neural activity and not in average amplitude, every spatial frame was normalized to zero mean and unit SD (Viana Di Prisco and Freeman

1985). Removal of amplitude artifacts from every spatial pattern tended to improve the resolution and separation of CS- patterns from CS+ patterns (Table 2, Time frame normalized data).

Spatiotemporal patterns from past work involved analyzing rabbit olfactory EEG bursts varying in temporal length from 75 to 200 ms (Freeman 1978, 1987; Freeman and Schneider 1982), or monkey visual cortical EEGs (Freeman and Van Dijk 1987). Recent results from human cortical

FIG. 7. Representative 120-ms segment of 64 visual cortical EEGs is shown from a chronically implanted 64-channel electrode array (left). After the traces were digitally band-pass filtered, 64 root-mean-square (RMS) values were calculated and plotted as a contour map (right).

FIG. 8. Examples of the 1st and 2nd modified fast Fourier transform (FFT) basis functions (*left*) and principal component analysis (PCA) temporal components (*right*) from the EEG traces in Fig. 7. The fraction of total variance of the EEG incorporated by the 1st component ranged from 60 to 70% for the FFT method and from 90 to 99% for the PCA method. The sums of all 5 FFT and PCA basis functions are compared (*bottom*) with the SEA of the EEG traces in Fig. 7.

EEG studies have demonstrated that there may be a diminishing return in terms of finding perceptual activity with analysis windows >175 ms in length (Menon et al. 1996). The relationship between experimental spatial pattern classification efficacy and the temporal length of the RMS analysis window was explored by varying the window length while classifying a well-characterized rabbit auditory cortical EEG data set (Freeman and Barrie 1993). Increasing the RMS window length from 10 to 500 ms yielded a tuning curve for the number of spatial patterns classifying correctly ($P < 0.01$) versus window length (Fig. 10, *top*, —). Classification values were calculated by stepping an n -ms window across 40 EEG records at intervals of 10 ms and subtracting the number of prestimulus patterns falsely classified from the number of poststimulus patterns correctly classified ($P < 0.01$). Classification values were plotted alongside the amount of computational time needed (on an Apple PowerPC 8100/80) to transform EEGs to spatial patterns for each RMS analysis iteration (Fig. 10, *top*, ---). The number of spatial patterns classifying below the 1% significance

level reached a plateau for a 150-ms RMS window and failed to improve thereafter, whereas the computational time steadily increased. Temporal resolution of periods of spatial pattern classification was concurrently studied in order to determine whether or not a certain analysis window length incorporated neural activity from neighboring discrete neural events, in effect blurring two or more separate events. Classification resolution was determined by calculating the average change in probability values with the use of Eq. 10. The hypothesis was that short temporal windows would yield spurious pattern classification resulting in a large Δp and that as the window length increased beyond 150 ms, individual neural events would become blurred, thereby yielding a low Δp . Calculation of Eq. 10 for a series of window lengths yielded a tuning curve for the resolution of discrete neural events (Fig. 10, *bottom*). The goal of this study was to maximize the number of patterns correctly classifying ($P < 0.01$), minimize computational time, and find some compromise between spurious and blurred neural event resolution. On the basis of the results from Fig. 10, a window length

TABLE 1. Comparison of spatial patterns of the dominant components from the two EEG decomposition methods with the RMS patterns

Correlation	Number Analyzed	Significant Matches	Percentage Matches
<i>A. Comparison of EEG decomposition techniques with visual neocortical patterns</i>			
RMS vs. PCA	9,000	8,918	99.1
RMS vs. FFT ¹	7,377	7,377	100
PCA vs. FFT ¹	7,377	7,300	99.0
RMS vs. FFT ²	9,000	8,764	97.4
<i>B. Comparison of EEG decomposition techniques with PPC patterns</i>			
RMS vs. PCA	6,750	6,348	94
RMS vs. FFT ¹	5,737	5,737	100
PCA vs. FFT ¹	5,737	5,123	89.3

Comparisons are made by nonparametric correlation of 9,000 neocortical and 6,750 prepyriform cortex (PPC) spatial patterns (120 ms). If the probability that the nonparametric correlation coefficient indicated a match between 2 spatial patterns was <0.001 ($P < 0.001$), then the criterion that those 2 spatial patterns were identical was satisfied. FFT¹ included only those records where the fast Fourier transform (FFT) decomposition was acceptable according to published criteria (Freeman 1987). FFT² included all FFT decompositions. EEG, electroencephalogram; RMS, root mean square; PCA, principal component analysis.

of 120 ms was adopted for the remainder of this study. This length served to capture short events without compromising the resolution of longer events. The time interval between analysis windows was chosen to be 20 ms. Shorter intervals increased computational time and provided no additional information regarding the temporal location of CS-/CS+ pattern separation. These findings generalized across all neocortical areas.

EEG fluctuations >100 Hz or <0.1 Hz were attenuated by analog RC filters. Within this range, digital temporal low-pass, high-pass, and band-pass filters were used to optimize spatial pattern resolution. Previous studies regarding the temporal digital filtering of raw olfactory bulb EEGs before RMS analysis had indicated the facilitated extraction of perceptually related spatial patterns of activity (Freeman and Viana Di Prisco 1986) by the removal of the low-frequency respiratory wave and the high-frequency fluctuations from the EEG time series. For the neocortical data sets no one set of band-pass filter settings could be applied a priori because the neocortical $1/f$ spectra gave no indication of the appropriate band onto which to lock filter settings. A low-pass temporal filter alone did not significantly alter the pattern classification levels by increasing the number of poststimulus CS- patterns that were distinguished from CS+ patterns. A high-pass filter with a low-cut component of 5–20 Hz, on average, increased the number of poststimulus patterns that were correctly classified, indicating that low-frequency EEG activity tended to mask spatial AM pattern stabilizing events. Therefore an optimal band-pass filter setting had to be derived on a per experiment basis by incrementing the low-cut parameter while keeping the high-cut setting constant at 100 Hz. After every new band-pass setting the data set was normalized and reclassified to evaluate CS-/CS+ pattern separation. Table 2, Temporally filtered

data, illustrates the degree of improvement in the number of patterns correctly classified above the 1% significance level for the pre- and poststimulus periods with a 100-Hz constant high-cut setting and a variable low-cut setting. Applying temporal filters to the raw EEG time series did not qualitatively affect the nature of the spatial pattern subsequently resolved, but only tended to improve the resolution of the individual CS- and CS+ patterns. This observation was supported by the $1/f$ form of the EEG time series, and the finding that each spatiotemporal pattern did not differ within the constant $1/f$ PSD domain (Fig. 9).

After a set of spatial patterns had been optimized with temporal filtering, the spatial spectra of those patterns was explored. Calculation of the average 2D PSD from PPC patterns (Fig. 11) closely matched previous results from the olfactory bulb (Freeman and Baird 1987). The lowest resolvable spatial frequency for the PPC array (interelectrode spacing 0.56 mm) was 0.18 cycles/mm. The small peak near 0.9 cycles/mm was an artifact dependent on the electrode spacing of the array; because the spatial sampling frequency of the PPC array was 1.79 cycles/mm, the artifact located at 0.9 cycles/mm was equivalent to the spatial Nyquist frequency. Average spatial spectra from neocortical data sets (Fig. 11) resembled the PPC spectra in the upward convexity of the curve over the low spatial frequencies but differed in resolution because of the 0.79 mm interelectrode spacing of the neocortical array. The lowest resolvable frequency for the neocortical data sets was 0.13 cycles/mm and the spectral peak near 0.62 cycles/mm was also an artifact reflecting the electrode spacing or the spatial Nyquist frequency for the neocortical arrays.

Log spatial PSDs calculated from the PPC and visual, somatic, and auditory cortices, when plotted against the log spatial frequency, were tested for conformity to a $1/f$ spatial spectra at >0.1 cycles/mm. Curves described by Eq. 2 were regressed onto the high-frequency segment of the 2D PSD data (defined as that between 0.1 and 0.9 cycles/mm for the PPC data and between 0.1 and 0.62 cycles/mm for the neocortical data) and plotted against the average PSD $\pm$ SE expressed to the 95% confidence level (Fig. 11). The criterion was adopted that the spatial spectra were $1/f$, if the regression curves lay within the SE curves. According to the results illustrated in Fig. 11, the majority of the PPC spatial spectra deviated from $1/f$, although the neocortical spectra conformed to $1/f$ for those spatial frequencies between 0.1 cycles/mm and the spatial frequency artifact at 0.62 cycles/mm. Spatial frequencies >0.62 cycles/mm formed a spectral tail significantly below the regression curve.

Previous studies had indicated that spatial digital filters applied to EEG spatial patterns increased the resolution of classifiable patterns from the olfactory bulb (Freeman and Baird 1987). The spatial digital filter parameter space was searched to determine whether the PPC and neocortical patterns could be better resolved. Band-pass spatial filters facilitated the resolution of spatial patterns by increasing the number of poststimulus patterns that correctly classified while concurrently decreasing the number of prestimulus patterns falsely classifying (Table 2, Spatially filtered data). Pre- and poststimulus classification figures represent the number of patterns classifying below the 1% level for each cortical

FIG. 9. Averages of Euclidean distances are shown between points in 64-space from normalized RMS reference patterns to normalized FFT PSD bin patterns from 40 CS- /CS+ prestimulus (*left*) traces and poststimulus (*right*) traces. Power within an FFT spectral bin had nothing to do with the spatiotemporal pattern resolved for that bin because every pattern was normalized before the calculation of Eq. 4. The graph shows the dependence of the spatial amplitude modulation (AM) patterns (expressed as points) on the frequency components of the carrier, which were derived from the FFT PSD at 2-Hz intervals. Standard errors at each frequency were used to determine the 99% confidence interval. Analyses of PSD patterns from visual (*top*) and somatic (*bottom*) experiments illustrated that all FFT PSD patterns reconstructed from the 20- to 100-Hz ($1/f$) portion of the spectra were equivalent, and that patterns within the low-frequency (2–20 Hz) range differed progressively with decreasing temporal frequency into the theta range. These results indicate that the aperiodic oscillation in each segment is a unitary event that cannot manifest a collection of limit cycle oscillators.

area. On average, the classification levels increased $\sim 50\%$ over the numbers attained with temporal filters alone. To test whether or not the process of spatially filtering the spatial patterns had induced any amount of artificial pattern classification, the spatially filtered data were renormalized and reclassified. There was no significant difference between the spatially filtered data and the renormalization of the spatially filtered data (Table 2, Spatially filtered, time frame normalized data).

For each experiment, across animals and sensory modalities, a statistically significant ($P < 0.01$) number of poststimulus patterns was correctly classified when compared with the prestimulus section of the same experiment (Table 2, Raw data). This finding conformed to previous results in the olfactory (Freeman and Grajski 1987; Freeman and Schneider 1982; Viana Di Prisco and Freeman 1985) and visual systems (Freeman and Van Dijk 1987). The poststimulus temporal location, within trials, of spatial pattern separation (CS- from CS+) was determined by plotting the probability values calculated with Eq. 9. On the basis of the number of CS- patterns correctly discriminated from CS+ patterns at any given time, a series of probability values was generated for each experiment (Fig. 12).

There were multiple temporal locations where the CS- and

CS+ spatial patterns were separately classified ($P < 0.01$) within the poststimulus section of each experiment. These took the form of a rapid sequence of multiple episodes of separation between 30 and 1,000 ms poststimulus, with the later peaks corresponding to periods where the animal's respiration increased in response to the CS+ stimulus (behavioral marker, CR). The time onset of the CR was $\sim 700 \pm 500$ (SE) ms poststimulus arrival. The temporal location of PPC pattern classification was found to be lagged when compared with the neocortical data sets, because of a 500-ms delay inherent in the olfactometer's air stream. The successive spatial patterns within each episode of pattern separation differed, as measured by a nonparametric correlation coefficient, from all patterns that preceded the period of classification and all patterns that were subsequently formed. For example, in Fig. 12 (prepyriform) there were two episodes where the CS- spatial patterns were significantly different from the CS+ patterns. The initial episode occurred at $\sim 4,100$ ms whereas the second episode was located at $\sim 4,600$ ms. Between these two episodes the CS- and CS+ patterns at 4,100 ms were not repeated (i.e., identical) at 4,600 ms.

Determination of whether or not peaks of significant pattern classification were due to a small sample size (40) was conducted by computing a cross-classification analysis of

TABLE 2. *Classification efficacy as a function of normalization and digital filtering*

Classification of Averages	Prepyriform (<i>n</i> = 11 experiments)		Visual (<i>n</i> = 6 experiments)		Somatic (<i>n</i> = 9 experiments)		Auditory (<i>n</i> = 14 experiments)	
	Pre-stim	Post-stim	Pre-stim	Post-stim	Pre-stim	Post-stim	Pre-stim	Post-stim
Raw data	0.91	3.45	1.83	24.5	2.22	30.0	2.36	6.43
Time frame normalized data	2.09	4.73	0.83	53.2	5.22	63.2	2.64	7.71
Percent difference from raw	+130	+36.8	−54.5	+117	+135	+111	+12.1	+20.0
Temporally filtered data	2.00	14.7	2.50	81.3	1.56	77.0	0.71	17.8
Percent difference from raw	+120	+326	+36.3	+232	−30.0	+157	−69.7	+176
Spatially filtered data	2.09	15.6	2.67	93.3	1.44	87.2	0.93	20.6
Percent difference from raw	+130	+353	+45.4	+281	−35.0	+191	−60.6	+220
Spatially filtered, time frame normalized data	2.00	17.7	2.83	92.2	1.11	88.7	0.71	20.7
Percent difference from raw	+120	+413	+54.5	+276	−50.0	+196	−69.7	+222

Improvements in levels of negative/aversive conditioned stimulus (CS−)/positive/rewarding conditional stimulus (CS+) classification of RMS patterns were obtained by time frame normalization, temporal filtering (100-Hz high-cut constant), spatial filtering, and renormalization. For raw data, the measure of classification efficacy was the average number of patterns classifying below the 1% significance level across the total number of experiments. The level of classification of the prestimulus segments was expected to decrease, whereas the level of poststimulus segment classification increased. For time frame normalized data, the RMS frames were normalized to zero mean and unit standard deviation (SD). This removed the frame-to-frame variation in amplitude, leaving only the pattern for classification. For temporally filtered data, band-pass temporal digital filters were optimized for each data set by stepping the low cut every 5 Hz and fixing the high cut at 100 Hz. The average number is shown of patterns classifying at <1% ($P < 0.01$) for the optimal temporal filter setting for each experiment, after normalization. For spatially filtered data, each experimental data set was filtered at its optimal temporal filter setting before spatial filters were applied. After temporal filtering and time frame normalization, band-pass spatial digital filters were optimized for each data set by incrementing the low cut and fixing the high cut at 0.624 or 0.880 cycles/mm (just below the spatial spectral artifact) for the neocortical and PPC experiments, respectively. For spatially filtered, time frame normalized data, after optimal temporal and spatial filter settings were found, each set of amplitude modulation (AM) patterns was reclassified after renormalization. These results reflect the finding that each segment has a center frequency that continually varies. The differing ranges of filters for optimal classification reflect the inhomogeneities of that variation across trials and sessions. For abbreviations, see Table 1.

two 100-record experimental data sets from the visual cortex. Multiple locations of significant ($P < 0.01$) pattern separation were observed in the 100-record experiments with no increase in spatial pattern resolution, demonstrating that earlier findings (Fig. 12, Visual) were not a function of small sample size.

Temporal sections of EEG data in which spatial patterns were significantly separated ($P < 0.01$) showed no distinctive features in the raw, non-normalized data. Figure 12 is representative of the locations of different CS−/CS+ spatial pattern separation after time frame normalization, temporal digital filtering, and spatial digital filtering, but as Table 2 demonstrates, the number of patterns correctly classifying as CS− or CS+ was dramatically lower when only the raw data was analyzed. Some experiments had no patterns classifying above the 1% level before normalization, thereby highlighting the need to remove global EEG amplitude biasing associated with a particular stimulus. Within the visual cortical experiments, there was a 117% average increase in the number of poststimulus patterns correctly classifying and a 54.5% average decrease in the number of prestimulus patterns falsely classifying (Table 2, Time frame normalized data) after removal of all global amplitude biasing by means of time frame normalization of each spatial pattern. Spatial pattern resolution was further increased via the elimination of low- and high-frequency EEG fluctuations within the temporal and spatial spectral domains. Poststimulus pattern resolution for the visual cortical experiments improved 270% after temporal and spatial digital filtering (Table 2, Temporally filtered data and Spatially filtered data).

During the search of the temporal digital band-pass filter parameter space, the criteria for filter component optimization included only maximizing the number of spatial patterns

correctly separated within the poststimulus experimental period and minimizing the number of patterns falsely separated within the control period. After the band-pass temporal filters had been optimized, each experiment was only filtered at one, optimal filter setting. Because the elimination of the 2- to 20-Hz EEG activity facilitated the resolution of the $1/f$ domain of patterns, and the $1/f$ domain (20–100 Hz) of patterns comprised the dominant number of patterns able to be separated, the 2- to 20-Hz domain of EEG activity was normally removed. The possibility still remained that patterns within the 2- to 20-Hz domain were able to be separated within some poststimulus periods, but the exclusion of parts of the 2- to 20-Hz temporal frequency range hampered the ability to resolve those spatiotemporal patterns for this study.

Spatial patterns were compared between experiments taken from wk 1 and wk 2 by calculating the centroids [$\bar{C}^{(m,j)}$], with the use of Eq. 6, from the 1st wk's experiment and subsequently using them to classify the spatial patterns [$\bar{V}^{(i,j)}$] reconstructed, with the use of Eq. 5, from the 2nd wk's experiment. By applying this method, we demonstrated that the patterns from wk 1 served to classify patterns relating to identical stimuli from wk 2. Use of centroids calculated from wk 1 or from wk 2 to classify patterns from wk 3 similarly did not succeed. The distinctive pattern of rapid episodes of pattern classification (Fig. 12) was absent during the interweek cross-classification of the spatial patterns reconstructed from the experiment where the CS−/CS+ contingency was reversed. Although the stimuli were unchanged, the spatial AM patterns were altered by the shift in context associated with each stimulus. There were still significant CS−/CS+ pattern differences within the experiment from wk 3 regardless of contingency reversal. These findings were similar to stable spatiotemporal patterns of EEG activity previously found in the olfactory bulb until response

FIG. 10. Relationship between the duration of the segment for RMS calculation and the spatial pattern classification efficacy. The number of prestimulus patterns classifying correctly ($P < 0.01$) was subtracted from the number of poststimulus patterns classifying correctly. The difference was plotted against segment duration (*top*, —) and against the computational time needed (with an Apple PowerPC 8100/80) with increasing RMS duration (*top*, ---). Solid vertical bar: 120-ms window. The changes in probability of CS-/CS+ pattern difference were summed, as the window was stepped along the 6-s traces, on the premise that short windows would capture sudden changes in pattern difference more readily than longer windows that spanned intervals of pattern shift (*bottom*, —). Spatial pattern classification levels were maximized with a 150-ms RMS window, but a shorter length of 120 ms gave better temporal resolution and lower computational time.

contingencies were changed (Freeman and Grajski 1987), and they also support recent findings that neocortical spatial patterns are slowly and measurably altered as a function of time (Barrie et al. 1994).

Spatial distribution of the EEG signal

Previous work had demonstrated that the contribution to the classification of EEG spatiotemporal patterns from the olfactory bulb was not enhanced or diminished by deletion of any one channel as a subset of the 64 recordings used to compute those spatiotemporal patterns (Freeman and Baird 1987). This finding was tested with the PPC and neocortical data by deleting groups of randomly selected channels in sets of 0, 2, 4, 8, ... 63 across 50 iterations for each set from a well-characterized section of an experiment, and then recomputing the cross-classification analysis. A running average was logged of the number of patterns classifying correctly after a certain channel had been deleted in respect to the number of times it was used. If any one deleted channel contained more stimulus-related EEG signal than average, the number of patterns classifying correctly would decrease on repeated classification analysis. Similarly, if a deleted channel contributed more noise than signal, then the number

of patterns classifying correctly would increase after its removal. The average number of patterns classifying correctly after any channel was removed remained within the 99% confidence limits. This indicated that every channel contained an equal amount of the spatial signal used to classify the data set.

The question was also asked as to how deletion of increasing numbers of the 64 channels impaired pattern classification. After deletion of randomly selected groups of channels, with 50 iterations of classification per number deleted, an average number of patterns classifying above chance levels (50%) was calculated across 1 s of pre- and poststimulus data. Correctly classified patterns ranged from two to three patterns above the chance level for the control period (Fig. 13, *top*) and from 7 to 3.5 patterns above chance for the test period (Fig. 13, *bottom*). The error bars reflect the 99% confidence levels. These results showed that spatial patterns from primary sensory cortices were significantly resolved by as few as 16 channels, but with a monotonic decrease in classification with diminishing number of channels. The spatial location of the selected or deleted channels was arbitrary.

DISCUSSION

The hypothesis guiding this study was developed for the olfactory system. It holds that the module of perception in each sensory modality is an area of cortex that is comparable in size with that of the olfactory bulb and cortex, on the order of 1 cm² and containing several thousand cortical columns. The microscopic activity of the cortical neurons coursing by action potentials through the neuropil gives rise to a macroscopic cortical state, which is expressed in a spatially coherent, broad-spectrum waveform that is modulated in amplitude (AM) with respect to the surface coordinates. It is also modulated in time, owing to repeated state transitions at irregular intervals lasting on the order of 0.1 s, which manifest rapid changes from one spatial pattern to the next, owing to the activity-dependent gain inherent in the sigmoid input-output curve of local populations. The patterns are constructed by the nonlinear synaptic interactions of neurons distributed over the entire area, and they are subject to changes by modification of the synaptic web and modulation of the excitability of neurons by neuromodulators. Patterns tend to recur in respect to prior learning, and they are accessed by the cortex through the microscopic sensory input from receptors, relayed through the thalamus for neocortices. This input is reexpressed in the macroscopic state as it guides the neuropil in the construction of a pattern that depends in part on the cortical neurons selected by the stimulus and in part on the synaptic web preformed by learning (Freeman and Viana Di Prisco 1986).

The distinction between the microscopic and macroscopic levels of activity is crucial to this study. The number of neurons that suffices to form a local neighborhood has often been estimated to be on the order of 10,000 neurons, which is appreciably larger than the number that can be accessed by recording pulse trains simultaneously from multiple electrodes with present techniques. The fraction of variance in the pulse train of each neuron that is covariant with the population waveform has been estimated to be <1 in 1,000

FIG. 11. Average spatial PSDs (—) and $\pm 95\%$ confidence intervals ($\cdots$) were calculated from 40 poststimulus windows of EEGs from the 4 cortical areas. Curves were regressed onto the domain of the spatial spectra from 0.1 to 0.9 cycles/mm for the PPC and from 0.1 to 0.62 cycles/mm for the neocortices. The peaks near 0.9 cycles/mm in the PPC spectra and 0.62 cycles/mm in the neocortical spectra lay at the spatial sampling (Nyquist) frequency determined by the interelectrode distances of the recording arrays.

(Freeman 1992b), so the present limit of ~ 100 neurons is 10 times too small. The local EEG potentials arise from thousands of neurons by their the synaptic currents that flow across the tissue resistance between the neurons and sum as scalar values (Freeman 1975, 1992a). That sum is an epiphenomenon like a noise, for it does not bind the cells together. The binding is done by the innumerable synaptic interactions between the neurons to give the local mean field of the ensemble. EEGs are signs of the macroscopic activity of populations, whereas the pulse densities in the populations carry the activity from one place to another. When multiple recordings of pulse trains are made simultaneously, the participation of neurons in populations is seen as covariances called "phase locking" (Gray et al. 1992), "binding" (Ecklorn 1991), "synfiring" (Abeles 1991), and "reverberation" (Amit 1989). Population "coding" is commonly conceived (Aertsen et al. 1994; Georgeopolis et al. 1986; Kruger 1990; McNaughton 1993; Rolls et al. 1989) as the scalar or vector sum of the pulse trains of a collection of neurons, which serves to represent a sensory or motor "feature" in some pattern. Macroscopic coding is a small fraction

of the variances in relative pulse frequencies that is covariant among all neurons in a local neighborhood; it is an element in an activity density function (Freeman 1975) extending over a cooperative domain of cortical neuropil.

Cortical output consists of the simultaneous pulse trains of all of the corticofugal axons during the time window of a given state or frame. Owing to putative spatial divergence and temporal dispersion in the tracts carrying the output to cortical targets, the output undergoes spatial integration, by which all activity not near the common instantaneous frequency and phase is smoothed and attenuated. By this mechanism the cooperative activity pattern constructed by the cortex is selected, and the microscopic sensory-evoked activity is attenuated. Where cortical output is transmitted to multiple targets, all targets receive the same input, but may select differing aspects depending on their own learned spatial patterns of excitability. If it can be shown that this model for perceptual dynamics holds for all modalities, then a solution may be facilitated for the problem of multimodal convergence and integration of perceptual activity in the thalamus, entorhinal cortex, frontal lobe, and elsewhere.

FIG. 12. CS-/CS+ pattern differences were expressed as the probability that correct classification under cross-validation was due to chance. The prestimulus differences were at chance levels. The poststimulus differences in each cortex revealed a sequence of brief episodes of declining significance after stimulus arrival, with a late increase in somatic experiments 0.5 s before the onset of the unconditioned stimulus. Each point represents 1 120-ms time frame. The onset of the conditioned response (CR) (an increase in respiration for all experiments) occurred at $\sim 700 \pm 500$ (SE) ms poststimulus arrival.

This conclusion, regarding the selection by the target of the cooperative activity over the microscopic residuals transmitted to it, has been confirmed for the olfactory cortex (Bressler 1984, 1987), including allowances made for the axonal transmission delays in the output pathway, but it remains to be demonstrated for neocortical targets. Descriptions of synchronous firing of units separated by substantial distances, even interhemispheric, remain anecdotal, and in any event cannot be explained as being based on axonal and synaptic transmission without an appeal to interactive population neurodynamics.

According to the present hypothesis the optimal site for electrode placement is at the pial surface, owing to the spatial integration over neighboring columns that, to some extent, mimics the smoothing in the output transmission. Narrowband oscillations in EEGs and in unit firing probabilities have been reported from depth recordings in the somatomotor cortex (Murthy et al. 1994; Sanes and Donoghue 1993) and visual cortex (Eckhorn et al. 1988; Gray et al. 1992). Other studies have failed to find oscillations or have found them uncommonly and without stable relationships to sen-

FIG. 13. Two graphs illustrate the effects of randomly deleting channels in groups of 1, 2, 4, 8, 16, $\dots$ 63 and then calculating the average number of patterns classifying better than chance levels. These graphs demonstrate that spatial patterns may be resolved almost as well as with a 16- or a 64-channel array and that the EEG is homogeneously distributed across the spatial aspect of the cortex.

sory or motor events (Ghose and Freeman 1992; Young et al. 1992). The concept of binding by phase-locking of oscillations or spike firing has been criticized on the grounds that the onset of synchrony is too slow, the number of periodically firing neurons is too few, and the number of spikes in each segment from each neuron is too few (Tovee et al. 1993; Young et al. 1992). Narrowband oscillations, by the present hypothesis, constitute transitory coherences or intermediate products of integration, which are not given as output, if their phase and frequency are inconsistent with the whole. Our failure to find narrow spectral peaks in surface EEGs is evidence not that such activity is absent in the depth, but that it is unlikely to form a significant part of the perceptual output. Its absence does not imply that cortex could not work with narrowband oscillations, but that it does not, perhaps because switching from each state to the next may be quicker and more reliable, if persistent "ringing" and "resonance" are disenanced by the use of a broad spectrum for perceptually significant transmissions.

The result that the classificatory information in EEGs is homogeneously spatially distributed is important for the hypothesis for several reasons. The transmitted pattern is not only independent of the topography of the input axons that guided its formation; it is also independent of the topography of the output axons to multiple targets, which largely is determined by the requirements of embryological development and not by ontological experience. The interfacing of an extremely varied set of input patterns with the varying requirements of the set of cortical targets offers a combinatorial problem of immense complexity for any attempt at modeling with switching networks. The modeling is elementary, when an AM spatial pattern is elicited by any of a class of equivalent inputs, and when the same AM pattern is sent to all targets.

Further, the precise location of experimental electrodes is no longer important with respect either to input or output topographies. As with distributed representation in a holo-

gram, the same information is present on every channel, and the resolution depends on the number available. Having no specificity in respect to the topography of the sensory arrays, the AM patterns are well adapted for integration into multi-sensory gestalts. Finally, the result offers a solution to the "binding problem" (Hardcastle 1994) in broader terms than its original conception (Milner 1974; von der Malsburg 1983). Sensory information is indeed refined by pre-processing and is manifested in the activity of "feature detector" neurons, but its effects are directed into the activity of all other neurons in the cortical area, not a select few, and the AM pattern output is shaped by the entire history comprising the context of that area, not by a hierarchical schema of elementary forms. Such schemata appear to be unlikely, owing to the lack of AM pattern invariance with respect to stimuli and their uniqueness in spatial form as they evolve within each subject. The larger question of whether any invariants for sensory inputs exist in memory stores within brains is addressed elsewhere (Freeman 1995).

Another conclusion from this study is that 16 channels can suffice for EEG pattern classification almost as well as 64. This outcome was not predicted from previous olfactory results, so it was necessary to use the larger number. Despite wider spacing of the electrodes and therefore a larger "window" onto the pial surface in search of boundaries for cooperative domains, no "edges" were detected for the spatial patterns, in the form of channels near the margins of the arrays having less information for the classification. Preliminary recordings in other rabbits with electrodes placed in multiple sensory areas have shown that the concomitant activities of the three neocortices, as expected, differ substantially in detail, indicating that boundaries for each area of cooperation must exist in some form, but the boundaries may fluctuate from each frame to the next in an unpredictable manner.

The structures and properties of the several dynamic systems generating these EEG patterns are not known in detail, although it is likely that, as in the case of the olfactory system, the interactions of excitatory, inhibitory, and modulatory neurons in large numbers and over diverse distances can be modeled with nonlinear ordinary differential equations. Large sets of such equations, when coupled with many forms of feedback, are typically governed by stable solution sets known as "attractors." The formal definition and description of an attractor require that the system be stationary and autonomous, and that it be watched long enough for it to settle into a basin of attraction. These conditions do not hold for cortex during perception, so that it is impossible to prove whether a given state, which is manifested by an AM pattern of an aperiodic carrier, manifests a strange attractor or an asymptotic approach to a point, periodic, or quasiperiodic attractor perturbed by noise from the Poisson-like continuous firing of individual cortical neurons. The question of whether the cortical dynamics is chaotic (Elbert et al. 1994) is not only unresolvable; at present it is unimportant. The issue is whether a mass of neurons forming an area of neuropil is capable of establishing spatial patterns of cooperative neural activity over areas far greater than the mean length of dendritic and axonal arbors, which have a characteristically broad-spectrum carrier, and which are formed and dissolved in time periods much shorter than their mean

0.1-s duration. The results from the present study show that these are reliable properties of laminated neuropil, and that the dynamics can take microscopic sensory input and transform it to a macroscopic pattern in preparation for multimodal perceptual integration in thalamocortical and limbic systems.

The authors thank B. Andrews, S. Baker, J. Chin, J. Leung, D. Graham-Squire, and S. Truong for invaluable assistance with the experimental preparation. We also thank B. Burke and H. J. Chang for review of the data analysis.

More information on the background and research interests of the authors may be obtained on the Freeman Lab WWW site by accessing: <http://sulcus.berkeley.edu> on the Internet.

This work was supported by National Institute of Mental Health Grant MH-06686.

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Received 17 April 1995; accepted in final form 22 January 1996.

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