

A neurobiological theory of meaning in perception.

Part 4. Multicortical patterns of amplitude modulation in gamma EEG

International Journal of Bifurcation & Chaos [2003] 13: 2857-2866.

Walter J Freeman

Brian C. Burke

Department of Molecular & Cell Biology
University of California
Berkeley CA 94720-3200 USA
dfreeman@berkeley.edu
burkeb@uclink.berkeley.edu

Key words: binding, gamma band, neurodynamics, phase transition, spatial EEG patterns, synchronization

Running title: Amplitude patterns of multicortical EEGs

ABSTRACT

The aim of this study was to find spatial patterns of EEG amplitude in the gamma range of the EEGs from multiple sensory and limbic areas that demonstrated multisensory convergence and integration. 64 electrodes spread in small arrays were fixed on or in the olfactory, visual, auditory, somatomotor and entorhinal areas of cats and rabbits. The subjects were trained to discriminate 2 visual and then 2 auditory conditioned stimuli, one reinforced (CS+), the other not (CS-). A moving window was applied to the 6-s records from 20 trials of each CS including a 3-s prestimulus control (CS0). The root mean square amplitude was calculated for each signal in the gamma range, so each window gave a point in 64-space. EEG patterns from the CS+, CS- and CS0 conditions gave 3 clusters of points in 64-space. The Euclidean distance of each point to the nearest center of gravity of a cluster served for classification and estimation of the probability of correct classification. The results showed that the gamma activity (35-60 Hz in cats, 20-80 Hz in rabbits) in all five areas formed global patterns of amplitude modulation (AM) in time windows lasting ~100-200 ms and recurring at 2-4 Hz, which were correctly classified above chance levels ($p < .01$). All areas contributed information to the AM patterns that served to classify the EEG epochs in the windows with respect to the conditioned stimuli. In conclusion, multisensory integration took place over the greater part of the hemisphere, despite lack of phase coherence among the gamma waves. The integration occurred rapidly enough that, within 300 ms of CS onset, activity in every sensory area was modified by what took place in every other sensory area.

1. INTRODUCTION

Two opposing views of cortical function have competed for 150 years [Freeman, 2003]. In the connectionist view the cortex in each hemisphere is a mosaic of specialized modules constituting nodes in a dynamic network. Each sensory, motor, and associational area has multiple dedicated nodes that serve to extract features of stimuli, organize facets of movement, or integrate representations of complex concepts. Each node occupies an assigned area of cortex. The function of each area during behavior is inferred from its pulses recorded with microelectrodes, or its local field potential with EEG or MEG (magnetoencephalogram), or its metabolic rate with imaging. A stimulus is thought to generate a signal in the sensory receptors that impacts nodes in the cortical network and causes a chain reaction as the evoked neural activity cascades from each node to the next, as well as recursively to nodes activated earlier. The signals transmitted between nodes are sought in the mean rates and time intervals of pulse trains, or in the phases and amplitudes of gamma waves generated by the transmitting and receiving nodes. In EEG studies connectionists have measured the time-intensity relations between pairs of cortical areas during performance of learned behaviors, in order to deduce the timings, strengths, delays, and directions of causal intercortical couplings. Some have used narrow band filtering with time-lagged correlation or autoregressive models [Sheer, 1976, 1998; Bressler, 1996; Mingzhou et al., 2000; Luu, Flaish and Tucker, 2000; Haig et al., 2000] such as 37-41 Hz, often with comparison of power in other bands (e.g., 33-37 Hz, 41-45 Hz to distinguish gamma EEG from EMG - scalp muscle potentials). Others have used coherence from broad band recording with Fourier decomposition of signals in time epochs ranging upward from 0.1 sec. Frequencies were selected in the gamma range, which varied with species [Bressler & Freeman, 1980], for studies in rabbit [Barrie, Freeman & Lenhart, 1996], dog [Dumenko, 2000], cat [Freeman, 1975], monkey [Freeman & van Dijk, 1987; Bressler, 1996], and human [Menon et al., 1995; Müller, 2000] for calculation of coherence and time-lagged correlation between pairs of signals.

In the holist view the entire cortex is regarded as a functionally integrated unit. In evidence Haig et al. [2000] described global phase locking of oscillations in the gamma range of scalp EEG. Several groups have described enhanced gamma activity at the scalp with varying degrees of localization in conjunction with semantic stimuli [von Stein et al., 1999], with visual stimuli [Miltner et al., 1999; Rodriguez et al., 1999; Müller et al., 1996], in a pattern recognition task by infants [Csibra et al., 2000], and in a delayed response memory task by adults [Tallon-Baudry et al., 1998]. A staccato mode of holist operation was suggested by a shifting dipole found in scalp EEG by Lehmann and Michel (1990). The dipole displayed sudden jumps at intervals in the theta range 93-7 Hz). The emergence of 'bursts' of gamma activity in scalp recordings has been postulated to be due to an underlying increase in synchronization of oscillations in widely distributed areas of cortex. Other observers have reported widespread changes in scalp EEG following changes in binocular rivalry attributed to switching between hemispheres [Kaernbach et al., 1999; Engel et al., 1999; Ngo et al., 2000]. Nunez [1981] devised a physical model to explain cooperativity over the entire cerebrum. Linear analysis is ill-suited for aperiodic EEG [Lachaux et al., 1999; Mingzhou et al., 2000; Nunez et al., 1997; Srinivasan et al., 1998]. Dumenko [2000] complemented Fourier analysis with factor analysis and 'nonharmonic analysis'. Tallon-Baudry et al. [1998] and Csibra et al. [2000] used time-frequency analysis with Morlet's wavelets to decompose EEG and detect 'induced' epochs of gamma activity that were not phase-locked to the stimulus onset.

The question at issue here is how global integration of signals deriving from sensory stimuli might be observed and measured in cortical EEG activity. As described in the preceding report [Freeman, Gaál & Jornten, 2003], the EEGs that were simultaneously recorded from multiple areas on average showed sustained high covariance with no consistent evidence for intermittent transmission with delays of signals between areas in time intervals predicted from behavioral control and correlation. Therefore, in the present report an alternative model was examined, that was based on the characteristics observed in sensory areas in the formation of wave packets. The premise was that each area of cortex retained a high degree of autonomy, while it participated in cooperative activity with all other areas, but to differing extents in different behaviors. In sensory areas the cooperation was revealed in the shared wave form of the cortical gamma oscillation, with the behaviorally related signal in a spatial pattern of amplitude modulation of the carrier wave. This concept was generalized to the multiple EEG samples recorded from the several sensory and limbic areas in search of AM patterns that differed with respect to conditioned stimuli (CSs) that subjects had been trained to discriminate. Whereas in sensory areas the percentage of shared variance in gamma EEGs usually exceeded 95%, over multiple areas the covariance averaged 50%. The nonlocal character of the information in the EEGs that supported classification of wave packets in sensory areas was demonstrated by deleting randomly selected channels and showing that the goodness of classification decreased with the number deleted, irrespective of which channels were removed. Similarly, the classification of global patterns with respect to CSs was examined by deleting whole areas one at a time to determine the effects on classification efficacy. All areas proved to be involved, whether the CS was visual or auditory, in spatial pattern shifts without significant changes in amplitude, that is, with spatial AM but usually not temporal AM.

Cats were chosen for this work, because in the study of multisensory perceptions (Gestalts) it was essential to include recordings from the entorhinal cortex, the site in mammals of multisensory convergence into the hippocampus for spatial and temporal orientation. Unlike the rabbit, the cat anatomy provided clean surgical access to the entorhinal area through a trephine opening in the skull at the back of the head for sliding a flat electrode array along the upper surface of the bony tentorium into the temporal fossa. The cats were better able than rabbits to form an appetitive conditioned reflex (CR) of pressing a bar for food instead of a CR with aversive reinforcement by weak electrical stimulation of the cheek, in response to auditory or visual CSs.

2. METHODS

The methods of surgical implantation, training, and recording have been described in detail [Gaál & Freeman, 1998; Freeman, Gaál & Jornten, 2003]. Spatial analyses were on 64-256 ms windows stepped at 64-128 ms over the 12-16 signals (after bad channel replacement) from each local array and then over all signals filtered initially in a pass band of 20-80 Hz as in rabbits. AM distributions were calculated from the 64 root mean square (RMS) values in each window, under the assumption of zero phase lag between all signals. The AM patterns were alternatively derived from the loading factors of the first component in Principal Components Analysis (PCA), performed over 64 channels (one epoch, trial and subject at a time after filtering to get the gamma range). The loading factors formed a 64x1 column vector for each AM distribution or AM pattern and specified a point in 64-space. Classification of RMS and PCA spatial distributions with respect to CS+ and CS- discrimination was undertaken to identify AM patterns related to behavior. Classification was done by breaking the set of 40 records from each session into a training set and a test set, each with 20 trials. The training set had 20 trials of 10 even-numbered CS+ trials and 10 even-numbered CS- trials that were used to calculate centroids for CS+ and CS- AM patterns in n -space, $n = 12$ to 64. The number of correctly classified AM distributions in the poststimulus set of 20 odd-numbered trials was determined. A poststimulus AM distribution was taken to be correctly classified, when the distance of its point to the correct training CS+ or CS- centroid was less than the distance to the incorrect training centroid. The classification procedure was repeated by reversing the training and test sets in cross-validation. The two numbers were added to give the total number, N , of correctly classified AM distributions in the window of 40 AM distributions. If the number, N , exceeded chance levels, the epochs correctly classified with CS were denoted 'AM patterns', to distinguish them from 'AM distributions' with no patterns [Freeman & Barrie, 2000].

In previous studies [Barrie, Freeman & Lenhart, 1996] the binomial distribution of N was used to determine the probability of classification by chance: $\geq 26/40$, $p < .05$; $\geq 28/40$, $p < .01$. AM patterns by this test were found only in the poststimulus period, not in the prestimulus control period. Classification better than chance levels was seldom found for individual cortices in the present study, in large part owing to the relatively small number of electrodes on each cortex: 12-16 instead of 64. As an alternative, the mean \bar{N} of the numbers, N , across subjects and sessions at each window was calculated at step in the control and poststimulus periods. \bar{N} at each step was divided by the fixed standard deviation of \bar{N} over the entire control period from the same session to give a normalized value, the 't:c-ratio'. The ratio was related to a t-value but without dividing it by the square root of the number of samples. The t:c-ratio at each time step gave a numerical assay of the differences between AM distributions from CS+ and CS- trials across subjects and sessions. The assay was used to construct tuning curves for classifier-directed optimization of the EEG filter pass band width, center frequency, window duration, and number of recording locations and channels.

From previous experience [Barrie, Freeman & Lenhart, 1996] the times of onset of AM patterns were expected to vary across trials between the onsets of the CS and CR. Yet the classification procedure searched across trials in a window that was stepped across all trials at the same time. The variation was termed 'jitter' by Tallon-Baudry et al. [1998]. It was dealt with here by

searching on every trial for an optimally classifiable AM pattern, which might occur before or after the 128 ms window that was fixed for all trials at each step.

First, 85 RMS AM distributions of the 64 signals were calculated for every trial in 64 ms steps across the 5.44 s remaining in 6 s trials after filtering. The AM distributions were stored and indexed in 2 matrices, one for a training set and one for a test set. As already explained, the CS+ and CS- training centroids were calculated from 20 AM training distributions in each window in steps of 128 ms through the control and poststimulus periods, reversing training and test sets in cross-validation. At each step \mathbf{N} was calculated from the 20 CS+ and 20 CS- AM test distributions within the window to their respective CS+ and CS- training centroids. The Euclidean distances for every AM distribution at each step were stored as baseline values, along with the 85 values of \mathbf{N} .

Second, on every trial in a step before and after the fixed window, the AM test distribution was recalled from storage by index. Its Euclidean distances to the two training centroids were calculated. The calculation was repeated for up to ± 5 steps (totaling ± 320 ms, which was ± 2.5 times the window duration). Trial by trial, the test AM distribution in the window was replaced by the test AM distribution in the adjacent step that had the lowest Euclidean distance to the correct one of the two training centroids in the current window. The substitution was repeated for all 40 trials, and the classification assay, \mathbf{N} , was re-calculated for that window and shift size. The entire procedure was repeated across the trials, but excluding the steps in the 160 ms intervals preceding and following the 3 s time marker for stimulus onset, in order to avoid mixing control and poststimulus AM distributions.

Third, new training centroids were calculated using the substituted AM patterns at the optimal offset, and the test sets were re-classified. The means and SD were re-calculated to give new values of \mathbf{N} and t:c-ratios. The procedure unavoidably re-used some of the same AM patterns in successive windows, so that the successive t:c-ratios were not from independent samples. Therefore, experimental significance was taken as empirical assays from the differences between the 3 s control and poststimulus periods in \mathbf{N} and the t:c-ratios.

3. RESULTS

3.1. Spatial patterns of gamma EEG in relation to conditioned stimuli (CS)

Spatial AM distributions of gamma EEG were measured and classified in search of episodic correlates of conditioned behavior comparable to those previously found in rabbits [Freeman & Viana Di Prisco, 1986; Freeman & Grajski, 1987; Barrie, Freeman & Lenhart, 1996]. Analysis was focused on time epochs located between the times of onset of CS and CR in blocks of 40 trials, 20 with CS+ and 20 with CS-, in which there might be significant differences between the EEG with respect to the two discriminated stimuli. As in rabbits, the neocortical EEG signals from cats on visual inspection revealed no significant alpha or theta waves nor any fluctuations in amplitude or phase over time that might serve to localize 'bursts' of gamma activity, such as those readily seen in relation to respiration in the bulbar EEG of both cats and rabbits. Accordingly as with rabbit EEG spatial analysis a window was stepped across the blocks of signals from each subject and trial. At each step on each trial the spatial distribution was expressed by a set of 64 root mean square (RMS) numbers constituting a 64x1 column vector that specified a point in 64-space.

The classification test was made at each step of the degree to which the 40 spatial distributions at that step could be correctly classified with respect to the antecedent CS+ and CS- stimuli by the clustering of the points in two hypervolumes localized within 64-space, both distinct from a third hypervolume containing points derived from AM distributions in the overlapping stepped windows in the 3 s pre-stimulus records of CS+ and CS- trials. Initially the data from all subjects and trials were normalized and pooled to establish a baseline of separation, and then the parameters of search were varied to determine optimal values for pre-processing the data from subjects and sessions separately. A normalized assay, the t:c-ratio (test:control ratio), of separation of AM patterns over the data set was derived by dividing the mean, \bar{N} , from each window by the mean of the standard deviation of the classification numbers, \bar{N} , from the entire control period.

Test of the unfiltered EEG in which the high power in the low frequency range dominated the forms of the spatial distributions did not reveal classification with respect to behavior. This outcome was expected from experience with rabbit data. The classification test on RMS values was repeated after band pass filtering in the gamma range and with a window duration of 64 ms that had served optimally for rabbits (20-80 Hz). No evidence for significant classification was found in the individual subjects and areas. A window duration of 256 ms gave elevated classification rates of AM patterns by RMS in the test period but not in the control period or in the first 250 ms after CS onset [dark trace in Fig. 1]. The efficacy of classification by using the loading factors of the 1st component from PCA [light trace] was less than that by RMS.

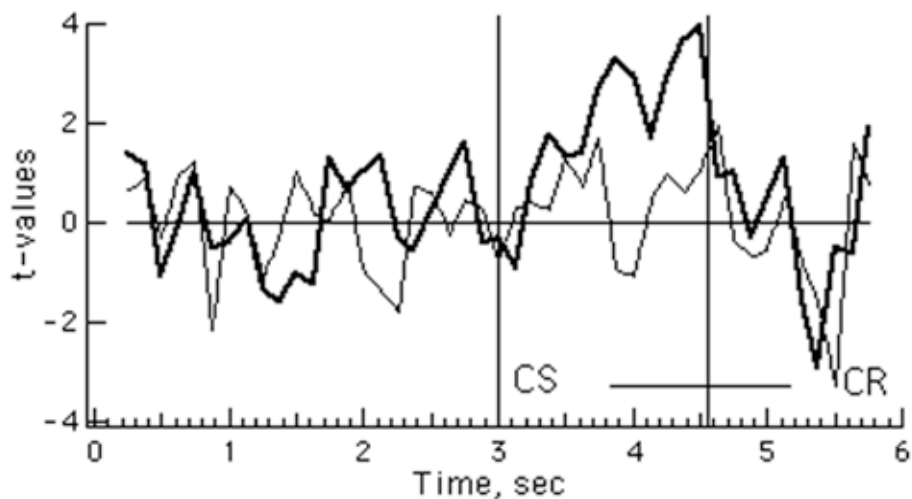


Fig. 1. The classification assay, $t:c$ -ratio (test:control), was calculated by dividing the number of AM patterns correctly classified in each window, \underline{N} , by the SD of the numbers, \underline{N} , in the entire control period for each subject and session. The window of 256 ms with step size of 128 ms revealed epochs of increased separation of AM patterns with respect to discriminative CS occurring in the interval between the CS and the CR.

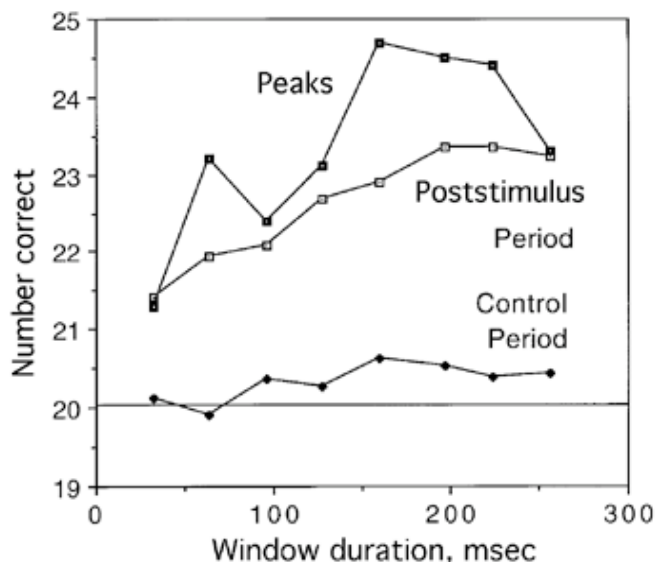


Fig. 2. The number of correctly classified trials out of the total of 40 trials was used as the criterion for a 'tuning curve' to determine the optimal window duration for comparison between the 3 s prestimulus control period and the 3 s poststimulus test period. The 'peaks' were the averages in the test interval of 3.6 to 4.4 s. Classification of AM distributions with respect to CS+ and CS- by root mean square (RMS) amplitude was statistically significant at correct counts of ≥ 26 ($p < .05$) and ≥ 28 ($p < .01$). These levels were seldom reached in data from individual subjects and sessions.

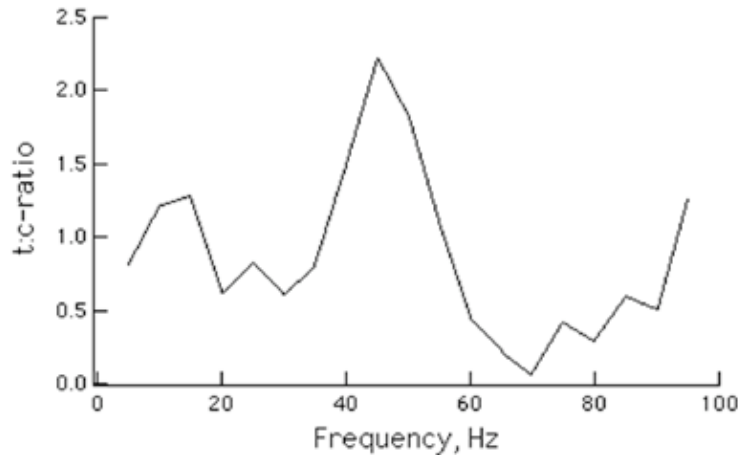


Fig. 3. The pass band width was fixed at 10 Hz, and the center frequency was stepped across the EEG spectrum to construct a tuning curve using t:c-ratios to optimize the band pass filter for the gamma activity.

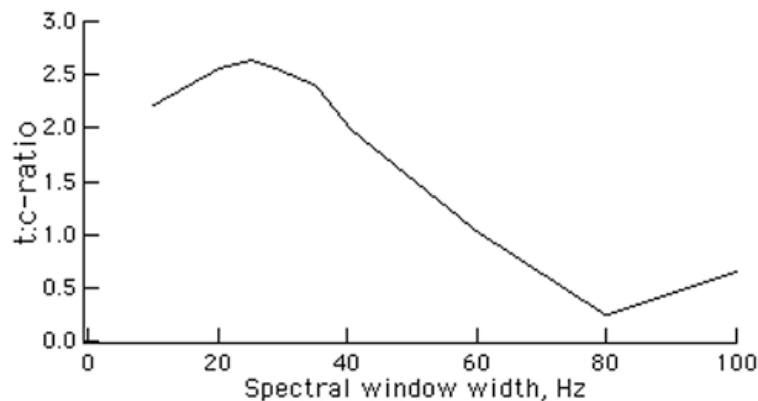


Fig. 4. The center frequency was fixed at 45 Hz, and the width of the pass band was varied in widths of differing size. The t:c-ratios were used to determine the optimal settings for the band pass filters.

With the t:c-ratio as an optimizing criterion, a series of 'tuning curves' was devised to determine the optimal values of search parameters. Fig. 2 shows the 'tuning curves' from varying the length of the window that was stepped across the data. The optimal window duration in the cat (128-256 ms) was longer than that previously found for the rabbit (80-100 ms). Fig. 3 shows the results of varying the center frequency in Hz of the pass band, and Fig. 4 shows the results of varying the width of the spectral pass band. From these assays the optimal pass band for the cat was determined to be 35-60 Hz. Classification of AM distributions from the individual subjects and sessions remained below statistical significance.

The assay including all subjects and sessions was repeated following deletion of data from each of the five sensory areas. Every deletion resulted in a decrease in level of classification [Fig. 5, light traces] below that from using all of the areas (dark trace). In no case either by individual or by the group was significant classification found in the 250 ms period immediately following CS onset, particularly in the sensory cortex to which the CS was directed.

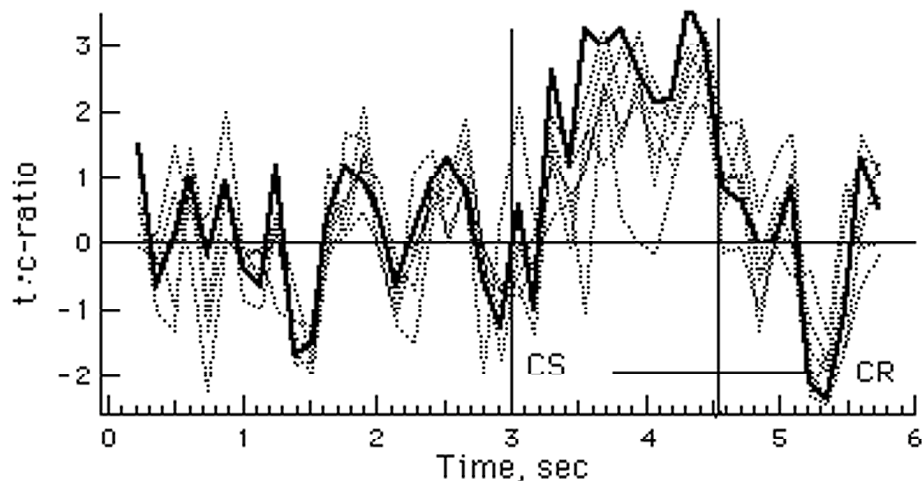


Fig. 5. Deletion of the EEG data from each cortical area reduced the classification assay in the test period but had no significant effect in the control period. The strongest effect was by removal of the olfactory signals, while the least was by deletion of the entorhinal signals. The window was 128 ms stepped at 64 ms. The mean t:c-ratios from the control period from 1.6 to 2.4 s and the test period from 3.6 to 4.4 s were derived after the deletions specified as follows. None: .34 vs. 2.71. EC: -.01 vs. 2.36. VC: .01 vs. 2.17. SM: .00 vs. 2.04. AC: .01 vs. 1.60. OB: .07 vs. 0.74.

Evidence from rabbit EEG had shown that the latencies of significant intermittent spatial AM pattern formation with respect to the time of CS onset varied across trials and subjects [Barrie, Freeman & Lenhart, 1996]. In order to trade classification efficacy for temporal resolution within the CS to CR period, the length of the window was reduced to 128 ms. The 40 trials in each session were divided equally into a training set and a test set. At each time step of 64 ms the CS+ and CS- centroids for the training set were fixed, and on each trial the Euclidean distance was determined first for the distribution in the test set within the time step and then for the distributions in windows up to 5 steps before and after that step. The AM test distribution closest to the correct training centroid was selected for the Euclidean distance assay. These sets of 20 new points in 64-space from CS+ and CS- trials were classified with the same centroids. The test set then became the training set for classification of the former training set, now serving as the test set in cross-validation. The substitutions gave sharper temporal resolution of the episodes of CS+ and CS- discrimination in the CS to CR interval [Fig. 6, dark trace] compared with none [light trace] but with some reduction in classification effectiveness owing to use of a short window duration. The optimal shift for this window duration was found to be ± 2 steps (± 128 ms). Visual inspection of the numbers of correct classification over the trial duration for each session and subject was undertaken in search of local maxima of classification, whether or not statistically significant. The time intervals between local maxima were measured and tabulated, giving an average and standard deviation of 196 ± 44 ms, placing the recurrence rate within the theta range (3-7 Hz).

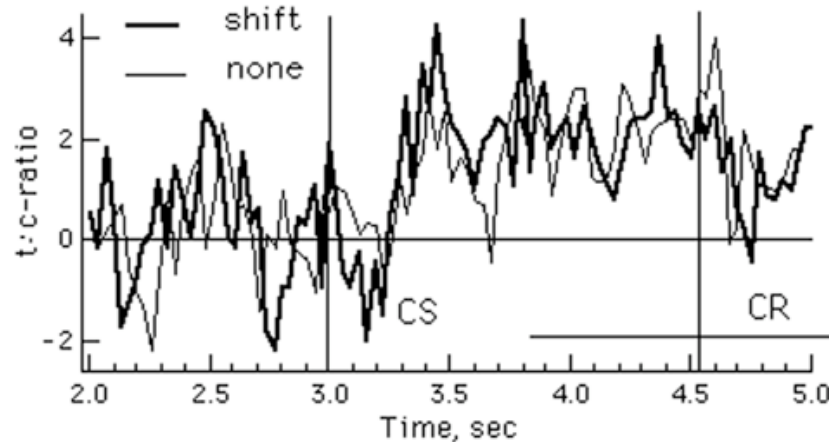


Fig. 6. The band pass filter settings improved the classification level and temporal resolution in the test period without significant change in the control period. The window duration was 128 ms, and the step size was 64 ms. The dark trace shows the classification level when all AM distributions were from RMS values in the same window. The light trace shows the effect of substituting AM distributions from neighboring windows before or after the centered window. Substitutions were based on the neighboring AM distribution having the shortest Euclidean distance to the correct centroid. The shift shown here was 2 steps, 128 ms.

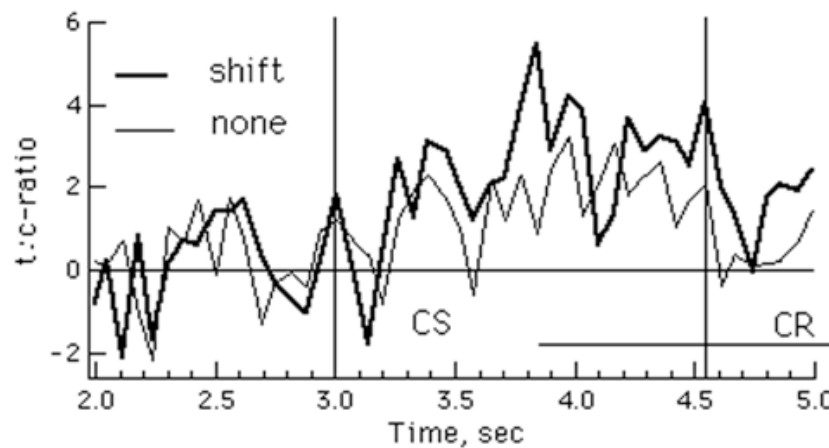


Fig. 7. Temporal resolution was reduced when the window width was increased to 256 ms with a step size of 128 ms. The classification assay in the test period increased further without significant change in the control period, when the centroids were re-calculated after substitution of the nearest neighbor AM distributions (± 1 step).

The entire procedure was repeated with a window duration of 256 ms and a step of 128 ms. The additional step was taken to re-calculate new centroids from a new training set containing the substituted patterns, before calculating the Euclidean distances of the test set and cross-validating. These changes reduced the temporal resolution and increased the classification assays [Fig. 7]. The optimal shift for this window was ± 1 step (± 128 ms as before).

4. DISCUSSION

The nonlinear model on which this study was based held that the AM patterns of mesoscopic wave packets were the raw materials from which macroscopic Gestalts were constructed. The analysis was predicated on the finding that the maximal values of time-lagged correlation between signals from pairs of cortices was at zero lag. The AM patterns were transmitted simultaneously by action potentials on numerous axons. These divergent-convergent pathways enhanced the signal-to-noise ratio by a spatiotemporal integral transform that performed generalization, and that removed extraneous sensory detail after it had selected the basin of attraction of the wave packet, thereby performing abstraction. The necessary condition was that the wave packet transmitted from each cortex be broadcast through the forebrain, where it overlapped with other wave packets. The broadcasting was enabled by several factors. First, the diameter of the wave packet ensured that the multiple information processing areas of each primary sensory cortex were included, each with its specific output connections. Second, the information by which the cortical output was expressed for transmission was spatially uniform in density [Fig. 16 in Freeman & Baird, 1987; Fig. 13 in Barrie, Freeman & Lenhart, 1996]. Each sensory area projected to multiple target areas, and every target received the same information. Whether the information was received could be determined by tuning in the receiving areas instead of by path-switching in the output connections of the transmitting cortex. Third, every neuron in the condensation disk of the wave packet participated in the transmission. Small world effects [Watts & Strogatz, 1998] could bring every cortical neuron within very few synaptic steps of every other. Wide spatial overlap of broadcast transmissions was expected, notably in the entorhinal cortex, which received input from all sensory areas directly or by synaptic stages as the basis for multisensory convergence and Gestalt formation [Freeman, 2001]. The model held that all cortical areas, irrespective of content, had the same form of expression of output: spatial and temporal amplitude modulation of a broad-spectrum carrier wave. The feasibility of convergence depended on the axonal integral transformation of transmitted information into the spatiotemporal frequency domain, prior to multisensory integration

Additional experimental work to test this hypothesis further is suggested in four directions. First, the failure of AM pattern classification to reach significant levels in the data from the individual subjects and sessions is the greatest weakness in the present results. The failure is most likely due to the small number of electrodes (12-16) for observing each area. Previous work [Freeman & Baird, 1987; Barrie, Freeman & Lenhart, 1996] indicated that 16 or more electrodes in each area would be required. Therefore, the experiments should be repeated with 128 or more electrodes. Measurements should be focused on the cortex to which the CSs are directed for comparison of the AM patterns in the first 300 ms after CS arrival with the later epochs in which multisensory integration is proceeding. Studies by Ohl, Scheich & Freeman [2000, 2001] in gerbil auditory cortex have shown that the spatial AM patterns in this early epoch retain topographic stimulus specificity, whereas those in epochs with longer latency do not. A significant failure of prediction was the poor performance of PCA. This should be re-explored with larger electrode arrays.

Second, transmission between cortices is predominantly polysynaptic. High-density electrode arrays should be placed along known directions of transmission, such as the dorsal and ventral streams between the visual cortex and its frontal and temporal targets, directly and through the

thalamus [Steriade, Curró Diossi & Contreras, 1993; Pedroarena & Llinás, 1997] in order to learn whether macrostates form by serial transmission through transmitter-receiver pairs resembling the bulb-prepyriform pair. Alternatively, small numbers of long axons by 'small world' effects [Watts & Strogatz, 1998] may support virtually instant macroscopic phase transitions throughout the neocortex of a hemisphere. The active hemisphere may simultaneously transmit the same macroscopic pattern to the other hemisphere and to the thalamus, basal ganglia and brain stem. The distinction between these alternatives may be made by distinguishing between areas that have phase cones like the olfactory bulb from those that do not like the prepyriform cortex [Freeman & Barrie, 2000]. At present a minimum of 64 electrodes on each area is required to detect and measure phase cones owing to the necessity for spatial low pass filtering, so that EEG systems having 256 channels [Tucker, 1993] or more will be required.

Third, an improved measure of the phase of gamma EEG with greater temporal resolution has been provided by the Hilbert transform giving the analytic phase [Tass et al., 1999; Freeman & Rogers 2002]. The results of its application to gamma activity have supported the nonlinear binding hypothesis at the mesoscopic level of wave packet formation. The global AM patterns reported here support the prediction that some degree of phase stabilization among oscillatory signals from multiple cortices should be found intermittently in the intervals between CS and CR, particularly in the presence of noise [Freeman, 1999]. Application of the Hilbert transform to these data has revealed epochs of global phase synchronization that include all of the areas here identified as maintaining AM patterns, with similar durations & recurrence rates [Freeman & Rogers, 2003]. The method should be applied to recordings from 128 to 256 electrodes in multiple high density arrays to search for phase cones simultaneously in multiple cortical areas and examine the question of timing among them. Preliminary evidence indicates that the onsets of global phase transitions may be synchronized, even if the gamma oscillations are not.

ACKNOWLEDGMENTS

This work was funded by research grants from NIMH (MH06686), ONR (N63373 N00014-93-1-0938), NASA (NCC 2-1244), and NSF (EIA-0130352). We express our gratitude to A. Halperin, J. Leung, and L. Jennings for help with surgeries and post operative care, K. Ahrens and A. Smart for helping to rebuild the switchboard connecting the recording cable to the amplifiers, and P. German for assistance during training and recording.

REFERENCES

- Barrie, J.M., Freeman, W.J. & Lenhart, Mark. D. [1996] Spatiotemporal analysis of prepyriform, visual, auditory and somesthetic surface EEG in trained rabbits. *J. Neurophysiol.* **76**: 520-539.
- Βρεσσλερ, Σ. Α. [1996] Ιντερραρεαλ σπνχηρονιζατιον ιν τηε πιουαλ χορτεξ. *Βεηαπ. Βραιν Ρεσ.* **76**: 37-49
- Βρεσσλερ, Σ. Α. & Φρεεμαν, Ω. Θ. [1980] Φρεθυενχηψ αναλψσις οφ ολφαχτορψ σψστεμ EEG ιν χατ, ραββιτ ανδ ρατ. *Ελεχτροενχηπη. χλιν. Νευροπηψσιολ.* **50**: 19-24.
- Csibra, G., Davis, G., Spratling, M.W. & Johnson, M.H. [2000] Gamma oscillations and object processing in the infant brain. *Science* **290**: 1582-1585.
- Δυμενκο, ζ. Ν. [2000] Τηε φυνηκτιοναλ σιγνιφιχανχε οφ ηιγη-φρεθυενχηψ χομπονεντς οφ βραιν ελεχτριχαλ ακτιπιτιψ. Ιν: *Χομπλεξ Βραιν Φυνηκτιονς: Χονχεπυαλ Αδψανχεσ ιν Ρυσσιαν Νευροσχιενχε.* Μιλλερ, Ρ., Ιωανιτζκιψ, Ι & Βαλαβαν, Π. (εδσ.). (Ηαρωοοδ Αχαδεμικ Πυβλ., Αμστερδαμ ΝΛ), πτ. 129-150.
- Engel, A.K., Fries, P., König, P., Brecht, M. & Singer, W. [1999] Temporal binding, binocular rivalry, and consciousness. *Consciousness & Cognition* [1999]**8**: 128-151.
- Freeman, W.J. [1975] *Mass Action in the Nervous System..* (Academic Press, New York).
- Freeman, W. J. [1999] Noise-induced first-order phase transitions in chaotic brain activity. *Intern. J. Bifurc. Chaos* **9**: 2215-2218.
- Freeman, W.J. [2001] *How Brains Make Up Their Minds.* (Columbia U.P., New York).
- Freeman, W.J. [2003a] A neurobiological theory of meaning in perception. Part 1. Information and meaning in nonconvergent and nonlocal brain dynamics. *Int. J. Bifurc. Chaos* **13**: 2493-2511.
- Freeman, W.J. & Baird, B. [1987] Relation of olfactory EEG to behavior: Spatial analysis. *Behav. Neurosci.* **101**: 393-408.
- Freeman, W.J. & Barrie, J.M. [2000] Analysis of spatial patterns of phase in neocortical gamma EEG in rabbit. *J. Neurophysiol.* **84**: 1266-1278.
- Freeman, W.J. & Burke, B.C. [2003d] A neurobiological theory of meaning in perception. Part 4. Multicortical patterns of amplitude modulation in gamma EEG. *Int. J. Bifurc. Chaos* **13**: 2857-2866.
- Freeman, W.J., Gaál, G. & Jornten, R. [2003c] A neurobiological theory of meaning in perception. Part 3. Multiple cortical areas synchronize without loss of local autonomy. *Int. J. Bifurc. Chaos* **13**: 2845-2856.
- Freeman, W.J. & Grajski, K.A. [1987] Relation of olfactory EEG to behavior: Factor analysis. *Behav. Neurosci.* **101**: 766-777.
- Freeman, W.J. & Rogers, L.J. [2002] Fine temporal resolution of analytic phase reveals episodic synchronization by state transitions in gamma EEG. *J. Neurophysiol.* **87**, 937-945.
- Freeman, W.J. & Rogers, L.J. [2003e] A neurobiological theory of meaning in perception. Part 5. Multicortical patterns of phase modulation in gamma EEG. *Int. J. Bifurc. Chaos* **13**: 2867-2887.
- Freeman, W.J. & Van Dijk, B. [1987] Spatial patterns of visual cortical fast EEG during conditioned reflex in a rhesus monkey. *Brain Res.* **422**: 267-276.
- Freeman, W.J. & Viana Di Prisco, G. [1986] Relation of olfactory EEG to behavior: Time series analysis. *Behav. Neurosci.* **100**: 753-763.
- Gaál, G. & Freeman, W.J. [1998] Relations among EEG from entorhinal cortex, olfactory bulb, somatomotor, auditory and visual cortices in trained cats. In: Ding, M., Ditto, W., Pecora, L., Spano, M. & Vohra, S., eds., *Proc. 4th Exper. Chaos Conf.* pp. 179-184. (World Scientific, Singapore).

- Ηαγ, Α.Ρ., Γορδον, Ε., Ωριγητ, Θ.Θ., Μεαρσε, Ρ.Α. & Βαηραμαλι, ΗΒ. [2000] Σψνχηρονουσ χορτιχαλ γαμμα-βανδ αχτιπιτψ ιν τασκ-ρελεεπαντ χορνιτιον. *ΝευροΡεπορτ* **11**: 669-675.
- Kaernbach, C., Schroger, E., Jacobsen, T. & Roeber, U. [1999] *NeuroReport* **10**: 713-716.
- Λαχηναξ, Θ.Π., Ροδριγυεζ, Ε., Μαρτινεριε, Θ. & ζαρελα, Φ.Θ. [1999] Μεασυριγγ πηασε σψνχηρονοψ ιν βραιν σιγναλσ. *Ηυμαν Βραιν Μαπινγ* **9**:194-208.
- Lehmann, D. & Michel, C.M. [1994] Intracerebral dipole source localization for FFT power maps. *Electroenceph. clin. Neurophysiol.* **76**: 271-276.
- Λυυ, Π., Φλαιση, Τ. & Τυχηρο, Δ.Μ. [2000] Μεδιαλ φρονταλ χορτεξ ιν αχτιον μονιτοριγγ. Θ. *Νευροσχιενχε* **20**: 464-469.
- Menon, V., Freeman, W.J., Cutillo, B.A., Desmond, J. E., Ward, M.F., Bressler, S.L., Laxer, K.D., Barbaro, N.M. & Gevins, A.S. [1996] Spatio-temporal correlations in human gamma band electrocorticograms. *Electroenceph. clin. Neurophysiol.* **98**: 89-102.
- Müller, M.M. [2000] Hochfrequente oszillatorische Aktivitäten im menschlichen Gehirn. *Zeitschrift für Exper. Psychol.* **47**: 231-252.
- Müller, M.M., Bosch, J., Elbert, T., Kreiter, A., Valdes Sosa, M., Valdes Sosa, P. & Rockstroh, B. [1996] Visually induced gamma band responses in human EEG - A link to animal studies. *Exper. Brain Res.* **112**: 96-112.
- Miltner, W.H.R., Barun, C., Arnold, M., Witte, H. & Taub, E. [1999] Coherence of gamma-band EEG activity as a basis for associative learning. *Nature* **397**: 434-436.
- Μιγγζηου, Δ., Βρεσσλερ, Σ. Α., Ψανγ, Ω. & Λιανγ, Η. [2000] Σηορτ-οινδω σπεχτραλ αναλψισ οφ χορτιχαλ επεντ-ρελατεδ ποτεντιαλσ βψ αδαππιε μυλτιπαριατε αυτορεγρεσσιε μοδεινγ: δατα προπροχεσινγ, μοδελ παλιδατιον, ανδ παριαβιλιτψ ασσεσμεντ. *Βιολ. Χψβεργ.* **83**: 35-45.
- Ngo, T.T.; Miller, S.M., Liu, G.B. & Pettigrew, J.D. [2000] Binocular rivalry and perceptual coherence. *Current Biol.* **10**: 134-136.
- Νυνεζ, Π.Α. [1981] *Ελεχτριχ Φιελδσ οφ τηε Βραιν: Τηε Νευροπψησιχσ οφ ΕΕΓ.* (Οξφορντ Υνιψ. Πρεσσ, Νεω Ψορκ).
- Νυνεζ, Π.Α., Σρινωασαν, Ρ., Ωεστδορπ, Α.Φ., Ωαφεισινγηε, Ρ.Σ., Τυχηρο, Δ.Μ., Σιλβερστειν, Ρ.Β. & Χαδυσχη, Π.Θ. [1997] ΕΕΓ χοηερενχηψ I: στατιστιχσ, ρεφερενχηε ελεχτροδε, πολυμε χονδυχτιον, Λαπλαχιανοσ, χορτιχαλ ιμαγιγγ ανδ ιντερπρετατιον ατ μυλτιπλε σχαλεσ. *Ελεχτροενηχεπηρο. χλιν. Νευροπψησιολ.* **103**: 499-515.
- Ohl, F.W., Scheich, H. & Freeman, W.J. [2000] Topographic analysis of epidural pure-tone-evoked potentials in gerbil auditory cortex. *J. Neurophysiol.* **83**: 3123-3132.
- Ohl, F.W., Scheich, H. & Freeman, W.J. [2001] Change in pattern of ongoing cortical activity with auditory category learning. *Nature* **412**: 733-736.
- Pedroarena, C. & Llinás, R. [1997] Dendritic calcium conductances generate high-frequency oscillation in thalamocortical neurons. *Proc. Nat. Acad. Sci. USA*: **94**: 724-728.
- Rodriguez, E., George, N., Lachaux, J.-P., Martinerie, J., Renault, B. & Varela, F. J. [1999] Perception's shadow: long-distance synchronization of human brain activity. *Nature* **397**: 430-433.
- Σηερο, Δ. [1976] Φοχυσεδ αρουσαλ ιν 40-Ηζ ΕΕΓ. Ιν: Κνιγητ, Ρ. Μ. & Βακκερ, Δ. Θ. (εδσ.) *Τηε Νευροπψηχηολογψ οφ Λεαροινγ Δισορδερσ.* (Υνιψ. Παρκ Πρεσσ, Βαλτιμορε ΜΔ), ππ. 71-87.
- Sheer, D. E. [1989] Sensory and cognitive 40-Hz event-related potentials: Behavioral correlates, brain function, and clinical application. In: *Brain Dynamics*. Basar, E. & Bullock, T. H. (eds.), (Springer-Verlag, Berlin).
- Σρινωασαν, Ρ., Νυνεζ, Π. Α. & Σιλβερστειν, Ρ. Β. [1998] Σπατιαλ φιλτεριγγ ανδ νεοχορτιχαλ δψναμηχσ: εστιματεσ οφ ΕΕΓ χοηερενχηε. *IEEE Τρανσ. Βιομεδ Ενγιν.* **45**: 814-826.

- Steriade, M., Curró Diossi, R. & Contreras, D. [1993] Electrophysiological properties of intralaminar thalamocortical cells discharging rhythmic (40 Hz) spike-bursts at c.1000 Hz during waking and rapid eye movement sleep. *Neuroscience* **56**: 1-9.
- Tallon-Baudry, C., Bertrand, O., Perronet, F. & Pernier, J. [1998] Induced β -band activity during the delay of a visual short-term memory task in humans. *J. Neurosci.* **18**: 4144-4154.
- Tass, P., Kurths, J., Rosenblum M, Weule J, Pikovsky A, Volkmann J, Schnitzler H, Freund, H. [1999] Complex phase synchronization in neurophysiological data. In: *Analysis of Neurophysiological Brain Functioning*, (ed. Uhl, C.), pp. 252-273. Springer-Verlag, Berlin).
- Tucker, D.M. [1993] Spatial sampling of head electric fields: The Geodesic Sensor Net. *Electroenceph. clin. Neurophysiol.* **87**: 154-163.
- πον Στειν, Α., Ραππελσβεργερ, Π., Σαρντηειν, Θ. & Πετσχηε, Η. [1999] Σψνχηρονιζατιον βετωεεν τεμποραλ ανδ παριεταλ χορτεξ δυοινγ μλτιμοδαλ οβφεχτ προχεσσινγ ιν μαν. *Χερεβραλ Χορτεξ* **9**:137-150.
- Watts, D.J. & Strogatz, S.H. [1998] Collective dynamics of 'small world' networks. *Nature* **394**: 440-442.